School of Pharmacy

The Patterns of Use and Economic Analysis of Antipsychotic Medications in Treating Hospitalized Psychiatric Patients

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This thesis is presented for the Degree of Master of Pharmacy of Curtin University of Technology

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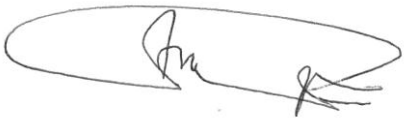
DECLARATION

To the best of my knowledge and belief this thesis contains no material previously published by any other person except where due acknowledgment has been made.

This thesis titled "The Patterns of Use and Economic Analysis of Antipsychotic Medications in Treating Hospitalized Psychiatric Patients" contains no material which has been accepted for the award of any other degree or diploma in a university.



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ABSTRACT

The objectives of the study were to (i) identify demographic and clinical characteristics of a cohort of psychiatric inpatients who were prescribed antipsychotic agents in Armadale Kelmscott Memorial Hospital (ii) evaluate the use of antipsychotics and other medications in treating these hospitalized psychiatric patients (iii) identify factors influencing prescribing patterns including patient-related characteristics such as age, gender and nature of condition(s) as well as the impact of different psychiatrist teams (iv) calculate the total cost of antipsychotics and other medications used in treating these patients and (v) calculate the total cost of hospitalization for this cohort of patients.

The medical records of hospitalized psychiatric patients who were treated with regular antipsychotic medications in 2005 were reviewed retrospectively. Data relating to patients' age, gender, principle diagnosis, medication details including drug name, frequency, route and number of dose administered, and length of therapy; laboratory tests related to monitoring of therapy and the treating psychiatrist teams were obtained from these records. The data were analyzed to determine the association between these demographic and clinical features, and also the patterns of clinical use of antipsychotic medications using the chi-squared test. Multinomial logistic regression analysis was also conducted to identify factors affecting the prescribing of different antipsychotics to admitted psychiatric patients. Data on the unit costs of medications, laboratory tests and bed days were collected for calculating the costs of antipsychotic, psychotropic, and all drug use; and the total costs. A one-way analysis of variance with post-hoc comparison was performed to determine whether age, length of stay, diagnosis and pattern of antipsychotic use influenced the costs of antipsychotic, psychotropic, and all drug use; and the total costs. In addition, the influence of gender and psychiatrist team toward these costs was analyzed with independent-samples t-test.

In this study the number of male patients was higher than the number of females and their mean age of all patients was 35.87±11.11 years. Almost half of the patients

were admitted to hospital for less than 10 days with the mean length of stay of 18.0 ± 18.3 days. The most common diagnosis was schizophrenia, followed by affective disorder (bipolar disorder and depression), drug induced psychosis and personality disorder. Patients treated by psychiatrist team A were hospitalized longer than those by team B and team A treated more schizophrenic patients than team B.

In terms of the use of antipsychotic medications, atypicals were prescribed more than ten times as often as typical drugs and around 30% of cases were on combination atypicals. Olanzepine, risperidone and quetiapine were the most frequent atypicals used. Other psychotropic drugs utilized in this study were benzodiazepines, mood stabilizers, antidepressants and anticholinergics. Antipsychotic, anxiolytic and hypnotic, and anticholinergic drugs sometimes were given as needed drugs.

Only diagnosis influenced the prescribing patters of antipsychotics. Patients with schizophrenia were treated relatively more commonly with risperidone and combination atypicals than patients with affective disorder and miscellaneous disorders. Meanwhile these latter disorders were treated relatively more frequently with olanzepine and quetiapine.

The highest total costs of antipsychotic, other drugs, and hospitalization were used by patients who were male, aged 35 to 44 years, had lengths of stay of more than 10 days, and had a schizophrenia diagnosis. Costs were also the highest in patients who were treated by psychiatrist team A and on combination atypicals.

The findings of this thesis in relation to the prescribing patterns of antipsychotic and other medications to psychiatric patients, the corresponding costs, and factors influencing prescribing patterns enables a better understanding to be gained of the profile of admitted psychiatric patients and their treatment. In a hospital environment with limited budgets, this information is useful for both psychiatrists and pharmacists in the future management of patients and in decisions relating to the allocation of the pharmacy budget.

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ABBREVIATIONS

AKMH	Armadale Kelmscott Memorial Hospital
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition
EPSE	Extrapyramidal Side Effects
HREC	Human Research Ethics Committee
ICD-10-AM	International Classification of Diseases and Related Health Problems-Australia Modification
LOS	Length of Stay
LSD	Least Significant Difference
MAOI	Monoamine Oxidase Inhibitor
MDD	Major Depressive Disorder
PRN	pro re nata
PTSD	Post-Traumatic Stress Disorder
SSRI	Selective Serotonin Reuptake Inhibitors
TD	Tardive Dyskinesia
TCA	Tricyclic Antidepressant
SNRI	Serotonin-Norepinephrine Reuptake Inhibitor
USA	United States of America

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1 Introduction

1.1 Background

Antipsychotic medications are frequently used by psychiatrists to treat psychotic illness and other psychiatric conditions, such as schizophrenia, manic phase of bipolar disorder, brief reactive psychoses, psychotic disorders due to a general medical condition, depression with psychotic symptoms, psychoses secondary to substance abuse (drug induced psychoses), mental retardation, and borderline personality disorders. [1, 2]

Antipsychotic medications are classified into two groups: the first generation that are called typical or conventional antipsychotics and the second generation that are called atypical antipsychotic agents.[3-5] Typical antipsychotics have a propensity to produce extrapyramidal side effects (EPSE) such as parkinsonism, dystonia and akathisia, and the longer term problem of tardive dyskinesia (TD).[2, 4, 5] Other side effects are associated with a reflection of receptor binding agents with potent H1 blockade that tend to be sedating, while those with peripheral anticholinergic (muscarinic) effects have a propensity to cause a dry mouth, constipation, urinary retention, and blurring vision, and those with alpha-adrenergic blockade can cause problematic postural hypotension. Other potential effects include weight gain, hyperprolactinemia, and lowering of the seizure threshold.[2, 4] Most atypicals are associated with substantial weight gain. [1, 2, 6] The use of these drugs is also associated with the onset or worsening of diabetes mellitus and hyperlipidemia resulting in increased risk of heart disease. [1, 2, 6]

The total use of antipsychotics has increased year by year, with the use of typicals decreasing and the use of atypicals increasing dramatically. [1, 7-9] Atypicals are being used in place of typicals because they can relieve negative symptoms and cognitive dysfunction in addition to controlling the positive symptoms of schizophrenia and they also cause less severe side effects, especially extrapyramidal side effects. [1-3, 10] Monotherapy upon discharge of atypical antipsychotics was found to be prescribed more frequently than typicals. In addition, there has been an increasing trend to use

combination typical and atypical antipsychotics and higher doses. [1, 2, 11-13] The Australian National Guidelines for treatment of first psychosis patients advocate the first-line use of atypical agents, and this practice is now commonplace.[14]

Patient demographics (gender, age and ethnicity), onset of illness, duration of illness, diagnosis of type and subtype of disorders, number of prior hospitalizations and culture affect antipsychotic efficacy for psychiatric disorders. [11, 15-17] These factors also influence the choice of medications and their dose.[11, 15, 18] However, the results of studies are inconsistent.[15-19] Several factors such as different diagnostic systems, heterogeneity of diagnoses, differences in sample selections, different length of follow-up periods, and failure to control for confounding factors may explain these inconsistencies. [15, 16]

Psychiatric illness has a large economic impact not only to the patients but also their families, caregivers, the health care system and society.[2, 20, 21] The greatest contributor of the cost of treatment and support of patients is hospitalization and medications have a major impact on this cost.[2, 10, 21, 22]

There is still limited evidence relating to the efficacy, tolerability, prevention of relapses, and pharmacoeconomic aspects relating to typical and atypical antipsychotics, although the second generation medications are far more expensive than the first.[1, 23] While the results of several studies have suggested atypicals are more effective and cost effective than typicals, [1, 7, 10, 17, 18, 24, 25] Rosenheck has argued that the results of several of these studies were questionable.[6] Reasons for this included the increase of drug manufacturer funded clinical trials, flawed study designs and misinterpretations of the research results.

Only a few studies have examined the use and cost of antipsychotics in Australia, and very few studies have examined factors affecting the choice of the medications and their doses. This study will take a cohort of psychiatric patients, those admitted to the Armadale Kelmscott Memorial Hospital in 2005, and analyze their use of antipsychotics and other medications, calculate the cost of treatment, and identify factors influencing the selection of antipsychotic medications.

1.2 Objectives

The objectives of the study were as follows -

1. Identify demographic and clinical characteristics of a cohort of psychiatric inpatients who are prescribed antipsychotic agents in Armadale Kelmscott Memorial Hospital.
2. Evaluate the use of antipsychotics and other medications in treating these hospitalized psychiatric patients at the Armadale Kelmscott Memorial Hospital.
3. Identify factors influencing prescribing patterns including patient-related characteristics such as age, gender and nature of condition(s) as well as the impact of different psychiatrist teams.
4. Calculate the total cost of antipsychotics and other medications used in treating these patients.
5. Calculate the total cost of hospitalization for this cohort of patients.

1.3 Significance

Prescribing patterns of antipsychotics have changed over time. This has cost implications for hospital budgets because the second generation treatments that are being used more widely are significantly more expensive than the first generation treatments, and there is a considerable difference in cost among the different second generation antipsychotic drugs. This study will provide information relating to the prescribing of antipsychotic medications and other medications to psychiatric patients so that a better understanding of prescribing patterns and their cost implication can be obtained. It will also provide information to identify factors influencing prescribing patterns. These factors may include patient-related characteristics such as age, gender and type of condition(s) as well as the impact of different psychiatrist team. The results of the study will be useful for both psychiatrists and pharmacists to use in the future management of patients. If differences are found between the prescribing behaviour of different psychiatrist teams, future research could investigate reasons underlying these difference

2 Literature Review

Then focus of the review of the literature is on psychiatric illness and its treatment. The chapter is structured as follows. Sections 2.1 and 2.2. present a background to psychiatric disorders and psychotropic medications respectively. Section 2.3 continues with a discussion of the use of antipsychotic medication including trends in its use. In Section 2.4, factors influencing prescribing decisions are covered, and in Section 2.5 the costs of treating psychiatric disorders is examined. Section 2.6 concludes with a discussion of the rationale for the present study, which examines the use of psychotropic medicines at a metropolitan hospital in Perth, Western Australia.

2.1 Psychiatric illnesses

Psychiatry is a branch of medical science that involves the diagnosis, treatment and prevention of mental illness and behavioral disorder such as depression, bipolar disorder, schizophrenia, anxiety disorders, personality disorders and the like.[26, 27]

Psychiatric or mental illness is any disturbance of emotional equilibrium, as manifested in maladaptive behavior and impaired functioning, caused by genetic, physical, chemical, biological, psychological, or social and cultural factors. It is also called emotional illness or mental disorder.[2, 26]

Most psychiatric illnesses cannot be cured. Some illnesses have short time courses with minor symptoms while other kinds of these diseases have chronic conditions and have a significant impact on patients' quality of life and life expectancy, and require long-term or life-long treatment. Efficacy of treatment for any given condition is also variable from patient to patient, and can result in complete resolution of symptoms or a poor or minimal response.[27, 28]

2.1.1 Schizophrenia and schizophrenia-like disorders

Schizophrenic disorders are one of a large group of psychotic disorders characterized by a distortion of reality, disturbances of language and communication, withdrawal from social interaction, and disorganization and fragmentation of thought, perception, and emotional reaction.[2, 21, 26, 29, 30] It may express behavior that is contrary to the original personality of the patient.[21, 26, 29] Most patients have both positive and negative psychotic symptoms. Positive symptoms include hallucinations, delusions and thought disorder; negative symptoms include anergia, flatness, and ahedonia.[5, 21, 26, 29, 30]

The condition may be mild or require prolonged hospitalization. No single cause of the disorder is known. Genetic, biochemical, psychological, interpersonal, and sociocultural factors are usually involved. Although slowly progressive deterioration of the personality may occur, dementia is not an inevitable consequence of the disorders. There may be recovery in some cases, and there may be relapse marked by intermittent episodes that begin after prolonged remission.[2, 3, 21, 26, 30]

Psychiatric disorders that are included in this category are schizophrenia, schizotypal disorder, persistent delusional disorders, acute and transient psychotic disorders, induced delusional disorder, and schizoaffective disorders.[31, 32]

The annual incidence of schizophrenia is between 0.1 and 0.5 per 1000 of the population with the point prevalence around 2.5 to 5.3 per 1000. Although the prevalence of schizophrenia is equal in men and women, women tend to have a later age of onset than men, and more benign course of illness, including fewer hospital admissions and better social functioning. The age of onset is between the age of 16 and 30 years. The peak onset for men is 15 to 25 years of age and 24 to 35 years for women.[2, 21, 29, 30, 32-34]

Antipsychotic medication is the mainstay of treatment for schizophrenia and for preventing relapses.[2, 21, 30] Antidepressant, mood stabilizers (e.g. lithium, valproic acid, carbamazepine), and benzodiazepines are commonly used for treating this disorder.[21]

2.1.2 Affective disorders

Affective disorders or mood disorders are a variety of conditions characterized by a disturbance in mood or affect as the main feature.[26, 29, 31, 35, 36] The central features of these syndromes are, on the one hand, depressed mood, pessimistic thinking, lack of enjoyment, reduced energy, and slowness and, on the other hand, elevated mood, over-activity, and self-important ideas. The former is called depressive disorder; the latter is called mania (or, if it is not severe, hypomania).[2, 29] The mood change is usually accompanied by a change in overall level of activity. Most of these disorders tend to be recurrent and the onset of individual episodes can often be related to stressful events or situation.[26, 31, 35] Psychotic symptoms, hallucinations and/or delusions related with a worse prognosis occur in both depression and mania.[35, 36]

Affective disorders comprise a group of related psychiatric and medical disorders, which include bipolar disorder, unipolar disorder, general anxiety disorder, manic episode, depressive disorder, cyclothymia and dysthymia.[29, 31, 36, 37] They are caused by an interaction between stressful events and other factors resulting from genetic contribution, childhood experience, physical illness, psychological, and biomedical disturbances.[2, 29, 36, 37]

The lifetime prevalence of mood disorders has been reported as 2 to 25%.[2, 33, 36] The prevalence of depressive disorder is 10 to 25% for adult women and 5 to 12% for men.[33, 36, 38] In the oldest group (≥ age 65), the prevalence is lower than the younger age groups.[32] The age of onset of major depression is around 27 years of age.[2, 32]

The prevalence of bipolar disorder is the same across sexes but type II (in which hypomanic and frequent depressive episodes occur) is more common in women than men.[32, 36, 39] The onset of this illness is adolescence and young adult, between 15 and 30 years old.[2, 32, 36, 39]

Management of affective disorder with drugs uses antidepressants, mood stabilizer and antipsychotics and often in combination. Lithium salts, carbamazepine, valproic acid formation and lamotrigine prevent recurrence of bipolar disorder.

Antipsychotics (e.g. risperidone, olanzapine, quetiapine) are for treating psychotic symptoms of affective disorders.[2, 36, 40, 41]

2.1.3 Drug- or substance-induced psychosis

In the tenth revision of the International Classification of Diseases and Related Health Problems-Australia Modification (ICD-10-AM), drug induced psychosis is included in mental and behavioral disorders due to psychoactive substance use category.[31, 42] It is a group of psychotic symptoms that occur during or following a long term-basis of alcohol or psychoactive substance use that may or may not have been medically prescribed.[27, 31-33, 42, 43] Substance intoxication or substance withdrawal with more severe symptoms than their common symptoms are included in this diagnosis.[31, 33, 42]

Substance use disorders are extremely common and frequently comorbid with other mental disorders. [38, 42] Beside psychosis, psychiatric disorders that frequently occur among patients with drug use problem are depression, anxiety disorders (particularly social phobias), and personality disorders.[3] In addition, many psychiatric patients also use drugs such as alcohol, cannabis, and amphetamines.[3, 21, 33, 38, 44] Alcohol and drug abuse may mimic a wide range of mental disorders and lead to misdiagnosis or misguided treatment.[38, 42] Treating both substance use disorders and comorbid mental disorders is essential to getting good outcomes.[38 44]

Abuse and dependence on substances are more common in men than in women, with the difference more marked for non-alcohol substances than for alcohol.[32, 33, 44] The highest prevalence rate of substance abuse is in the 18 to 24 year age group.[33]

Identifying the substances involved is crucial in treatment of this illness, Therapy with antipsychotic drugs such as olanzapine and haloperidol for immediate and short–term control of psychotic or aggressive behavior may be needed. For controlling agitation and anxiety, benzodiazepines may also be useful.[33, 43, 44]

2.1.4 Personality disorders

The Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) defines a personality disorder as "an enduring pattern of inner experience and behaviour that deviates markedly from the expectations of the individual's culture, is pervasive and inflexible, has an onset in adolescence and early adulthood, is stable over time, and leads to distress or impairment" (p. 629).[32]

People suffering these disorders usually refuse psychiatrist help and recovery is difficult because they do not recognize their symptoms. They often have problems in work and in social behavior. [33, 35]

These disorders have an onset in childhood, adolescence or early adulthood and are relatively chronic and stable throughout adult life.[32, 33, 35] Of the general population, around 10 to 15% would be diagnosed with a personality disorder. [35] The prevalence of personality disorders within clinical settings is about 50% and 60%.[32]

In DSM-IV these disorders are classified into three groups. Cluster A consists of paranoid, schizoid, and schizotypal personality disorders. This group is more commonly suffered by people who have biological relatives who are schizophrenic and seem odd and eccentric.[33, 35] Paranoid personality disorder is more common in males than in female.[32] Cluster B involves antisocial, borderline, histrionic, and narcissistic personality disorders, with borderline personality disorders being the most prevalent within hospital clinical settings. People with these disorders seem dramatic, emotional and erratic. Approximately 15% of all psychiatric inpatients (51% of inpatients with a personality disorder) and 8% of all psychiatric outpatients (27% of outpatients with a personality disorder) have a borderline personality disorder. Approximately 75% of persons with this disorder will be female.[32] The disorder is often diagnosed in children and adolescents. Anti social personality disorder is much more common in males than in females. Cluster C covers avoidant, dependent and obsessive-compulsive personality disorders. People with these disorders often seem anxious or fearful. Both cluster B and C apparently have a genetic base.[33, 35]

Antipsychotic medications (olanzapine, risperidone, haloperidol), antidepressants (tricyclic antidepressants, selective serotonin re-uptake inhibitors) and mood stabilizer may be used for the treatment of personality disorders, especially for borderline personality disorder.[35]

2.1.5 Other psychiatric disorders

In this study all psychiatric disorders other than the four diagnoses previously mentioned were classified in the "miscellaneous" category. Disorders included in this category are organic (including symptomatic) mental disorders, which have an etiology in cerebral disease, brain injury, or other insult leading to cerebral dysfunction; neurotic, stress-related and somatoform disorders; behavioral syndromes associated with physiological disturbances and physical factors; and disorders of psychological development.[31]

2.2 Psychotropic medications

Psychotropic medications are drugs that affect the mind, emotions and behavior.[26] These drugs act directly or indirectly on the central nervous system to affect mental and emotional processes. Psychoactive and psychopharmacology are alternative terms.[37, 45]

Psychotropic medications are used to treat mental illness. They are mostly synthetic compounds, although some are naturally occurring. They sometimes have adverse side effects that may reduce patients' drug compliance. Some of these side effects can be further treated by using other drugs such as anticholinergic (antimuscarinic) medications.[2, 29, 38, 46]

Psychotropic medications are commonly grouped as antipsychotic medications, antiparkinsonian or anticholinergic medications, anxiolytic and hypnotic medications, mood stabilizers, antidepressants, and various other types of medications, such as those used in the treatment of substance misuse and dementia[3, 38, 45-47]

2.2.1 Antipsychotic drugs

The term antipsychotic is applied to a group of drugs used to treat psychosis. These drugs are the cornerstone of treatment for schizophrenia and other psychotic disorders and work to reduce psychotic symptoms and prevent relapses.[2, 5, 21, 38] They are also effective in the treatment of other psychiatric disorders, such as bipolar disorder, depression with psychotic features, personality disorders, substance-induced psychotic disorder.[2, 33, 35, 36, 38, 48]

All antipsychotic drugs tend to block the D2 receptors in the dopamine pathway in the brain so the normal effect of dopamine release in the relevant synapses is reduced. The range of interactions can produce different adverse effects.[2, 3, 5, 49]

There are currently two main types of antipsychotics in use, the typical antipsychotics and atypical antipsychotics.[3, 5] Both types of antipsychotic drugs are efficacious and the differences among them are only in their potency (the dosage needed to produce the desired effect) and side effects.[2, 38]

2.2.1.1 Typical antipsychotic medications

The typical antipsychotic drugs are now out of patent so that any pharmaceutical company is legally allowed to produce cheap generic versions of these drugs. This makes them a great deal cheaper than atypicals, which are still in patent.[3, 5]

Typical antipsychotics are not particularly selective and also block the D2 receptors in the mesocortical pathway, tuberoinfundibular pathway and the nigrostriatal pathway. Blocking D2 receptors in these pathways is thought to produce some of the unwanted side effects (extrapyramidal side-effects) of the typical antipsychotic medications.[2, 3, 30, 47, 49] D2 blockade also leads to increased prolactin levels and associated sexual dysfunction.[2, 30]

Among the older antipsychotic drugs, drugs that are the most potent (e.g., haloperidol) tend to produce more extrapyramidal side effects, and those that are less

potent (e.g., chlorpromazine) produce more sedation, postural hypotension, and anticholinergic effects.[5, 38]

Typical drugs include chlorpromazine, pericyazine, thioridazine, droperidol, haloperidol, zuclopenthixol and pimozide.[3, 5, 19, 38]

2.2.1.2 Atypical antipsychotic medications

Atypical antipsychotic drugs are preferred as a first line treatment of psychosis due to the fact that they are believed to have fewer side effects and seem to have additional benefits for the negative symptoms of schizophrenia.[2, 3, 5, 50, 51]

Atypical antipsychotics have a similar blocking effect on D2 receptors but seem to be a little more selective than typicals. They act preferentially on mesolimbic rather than nigrostrial neurons. They also block or partially block serotonin receptors. This combination of effects on both dopamine and serotonin receptors might be the reason atypical antipsychotic drugs tend to have fewer extrapyramidal side effects than typical medications and have an additional effect on the negative symptoms of schizophrenia.[2, 3, 5, 19] Although they are less likely to cause extra pyramidal side effects, these drugs cause weight gain, hypotension, type II diabetes, elevation of cholesterol, triglycerides, and glucose serum level.[2, 5, 30, 52]

Amisulpride, aripiprazole, clozapine, olanzapine, quetiapine, risperidone and ziprasidone are all atypical antipsychotics.[2, 3, 13, 19, 47]

2.2.2 Anti-depressants

The mode of action of antidepressants is determined by receptor-mediated signal transduction in serotonergic or noradrenergic pathways. Treatment of major depression is the main role of these drugs. They are also indicated for treating other psychiatric disorders. These drugs combined with psychological therapies are used in the treatment of anxiety disorder, panic disorder, obsessive compulsive disorder, agoraphobia, social phobia (social anxiety disorder) and bulimia nervosa, in addition

to other indications such as chronic pain.[3, 35, 38, 41] Antidepressants are of use when a depressive component of the personality is present.[33, 35, 41]

Onset of the response of all antidepressants usually takes at least 1 to 2 weeks.[3, 47] It is preferable to commence at a low dose, and then increase to the minimal dose likely to be effective to see if there is a response, rather than to escalate rapidly and often unnecessarily.[3] Combinations of antidepressants have not been shown to be more effective than monotherapy, and there is a significant risk of serious adverse effects. In addition, the risk of dying in the event of overdose is increased. [3] Individual drugs differ in their adverse effect profiles, their potential for drug interactions, and their safety. This is critical in selecting which antidepressant to use.[3, 38, 47]

The first line of treatment should be a newer antidepressant including the selective serotonin reuptake inhibitors (SSRIs) (e.g. sertraline), mirtazapine, moclobemide, reboxetine, and venlavaxine.[3, 36, 38] Although most of the newer antidepressants may initially cause agitation, insomnia, nausea, and headache, and over time, sexual dysfunction, among other side effects, they are generally safer and more tolerable to patients than the older tricyclic antidepressants (TCAs) such as amitriptyline and imipramine; and irreversible nonselective monoamine oxidase inhibitor (MAOIs), such as phenelzine and moclobemide. [3, 38]

SRRIs such as sertraline and fluoxetine are effective for the treatment of major depressive disorder (MDD). Mirtazapine is also an efficacious antidepressant with faster onset of action than SSRIs based on comparison trials.[38] Mirtazapine is not associated with adverse cardiac effects and has been safe in overdose. It is quite sedating and thus generally administered at bedtime. Mirtazapine has been successfully combined with SSRIs and venlavaxine for partial responders or nonresponders to the other drugs.[38]

The safety and side effect profile of venlafaxine, a serotonin-norepinephrine reuptake inhibitor (SNRIs), is generally similar to that of the SSRIs. Like other newer agents, venlafaxine is safer in overdose than older agents. Venlafaxine represents an alternative to tricyclics and is considered to have similar efficacy profile but a more favourable acute and long-term side effect burden. Some clinical trial data suggest

that the rate of remission with venlafaxine can be higher than for some of the SSRIs for populations with relative more severe and melancholic depression.[38, 41]

The main negative aspects of TCAs use are their anticholinergic, postural hypotension, sedating properties and cardiovascular adverse effects in susceptible individuals or in overdose.[3, 38, 41]

Second-line therapy with TCAs, mianserin, and MAOIs would in general only be used after unsuccessful trials of several first-line antidepressants. It should also be noted that some patients, particularly those with severe or melancholic depression, only respond to second-line therapy.[3, 41]

2.2.3 Mood stabilizers

The term mood stabilizer is used widely for drugs used in the treatment of bipolar disorder. In general, mood stabilizers are a drug that is effective for the acute treatment of mania and/or bipolar depression, a drug that prevents episodes of mania and/or bipolar depression and a drug that possesses both of these clinical profiles.[3, 38] The drugs that are included in this group are carbamazepine, lamotrigine, lithium and sodium valproate.[3, 36, 41]

The best established mood stabilizers are lithium and the anticonvulsant, valproate.[36, 38] Lithium has been the mainstay of treatment for bipolar disorder for the past three decades but its serum concentration should be carefully monitored as it has a narrow therapeutic index.[3, 38] Many experienced clinicians find that valproate has efficacy equivalent to that of lithium but greater acceptability to many patients based on side effects and ease to use.[38]. Valproates also are found to be more efficacious than lithium among manic patients with mixed symptoms.[39] Therefore, it also has become a first line treatment, although greater overall benefit may still rest with lithium. [41]

Newer anticonvulsants and the second-generation antipsychotic drugs have also shown an effect as mood stabilizers.[38, 41] Carbamazepine is an effective alternative treatment for manic episodes when lithium or valproate is ineffective, contraindicated, or not tolerated.[38, 39]

2.2.4 Anxiolytics and hypnotics

Anxiolytics are drugs used primary to treat episodes of anxiety.[3, 41, 53] Common kinds of anxiolytics include barbiturates, benzodiazepines, zolpidem, zopiclone and buspirone.[3, 26, 54]

Benzodiazepines also have antiepileptic, muscle relaxant and memory impairing actions. The main disadvantage of benzodiazepines is physical dependence and they can impair performance and affect judgment so that driving and other skilled tasks can be impaired. These compounds are effective in relieving anxiety symptoms and can induce sleep. Problems arising from the use of benzodiazepines include overdose, particularly from the use of benzodiazepines together with other sedative drugs, and dependence as a result of long-term use.[3, 47] In acute psychotic episode, anxiety, agitation and insomnia can be treated with short term benzodiazepine therapy to achieve the appropriate level of sedation.[3, 41, 54]

Buspirone has little sedative effect and its most common adverse effects are drowsiness, dizziness, dysphoria, lightheadedness, nausea and headaches. There is no cross tolerance between buspirone and benzodiazepines, and buspirone cannot be used for benzodiazepine withdrawal.[3]

Zolpidem and zopiclone have similar sedative properties to the benzodiazepines but minimal anxiolytic, muscle relaxant and anticonvulsant properties. They are used as hypnotics in the short-term management of insomnia. Compared with benzodiazepines, they generally cause less morning sedation and do not affect normal sleep patterns. They are fewer reports of dependency or illicit use by substance abusers. Common adverse effects include diarrhea and dizziness (zolpidem) and bitter taste (zopiclone).[3, 47]

Pharmacotherapy is useful in dealing with agitation and anxiety in paranoid personality disorder.[54] In most cases an antianxiety agent such as diazepam is sufficient. But it may be necessary to use an antipsychotic, such as thioridazine, or haloperidol in small dosages and for brief periods to manage severe agitation or

quasi-delusional thinking. The antipsychotic drug pimozide has been successfully used to reduce paranoid ideation in some patients.[33, 35, 36]

2.2.5 Anticholinergic drugs

Anticholinergic drugs with central anticholinergic action are used to reduce some extrapyramidal effects caused by antipsychotics. Drug-induced parkinsonism, dystonia and akinesia respond reasonably well, but tremor respond less and akathisia has poor response. Antiparkinsonian drugs include benztropine, benzhexol, biperiden and orphenadrine. Benztropine can be sedating.[1, 3, 38, 54]
Routine administration of anticholinergic drugs with antipsychotics is not generally favored except when parenteral administration of high potency typical antipsychotics is being undertaken.[3, 38, 54] The reasons are some patients develop adverse effects to the antiparkinsonian drug, not all patients develop extrapyramidal adverse effects to antipsychotics and abuse of antipsychotics is frequent.[1, 3, 54]

If a high-potency traditional antipsychotic drug is used, an anticholinergic drug often should be added as prophylaxis against dystonia. [3, 38, 54] Benztropine may be preferred because it lacks the antishitaminic effects and it may be given at a dose of 2 mg twice a day.[3, 38]

2.2.6 Drugs used in alcohol and drug disorders

Therapy for patients with substance disorders are used in the detoxification and management of withdrawal symptoms; and also the treatment for co-occurring mental disorders.[38, 43, 55]

Acamprosate and disulfiram are used to reduce relapse after detoxication in patients with alcohol dependence. In some people it reduces alcohol craving, some of these people remain abstinent, others drink less alcohol.[3, 55] It is important that acamprosate is only used as an adjunct to psychological and social treatments because the long-term benefits of acamprosate are unclear. Disulfiram is used in the treatment of alcohol dependence in highly motivated, and compliant patient.[3, 38, 55, 56]
Person undergoing withdrawal or experiencing hallucination or delirium are treated

with antipsychotic drugs.[38] Mild illusion may be treated with benzodiazepines.[43, 55] Anticonvulsants such as carbamazepine, valproic acid, and gabapentin have also been used in the treatment of alcohol withdrawal. Thiamine deficiency is not uncommon in alcoholics experiencing withdrawal symptoms due to their poor dietary practices. Patients should receive thiamine, 100 mg daily, at the start of treatment.[3, 38, 56]

Buprenorphine is a partial opioid agonist used in the treatment of opioid dependence. Compared with methadone it has the advantage of lower overdose risk and less physical dependence. It is normally administered sublingually once daily.[3] The doses of buprenorphine and methadone need to be determined individually.[3, 38, 55]

2.2.7 Other drugs used in psychiatric illness

Psychostimulants can produce central nervous system stimulation. They are currently approved only for the treatment of attention deficit disorder with hyperactivity (ADHD) and for narcolepsy[3, 38] Their efficacy in ADHD has been demonstrated in all age groups, in which it has been shown to reduce hyperactivity. These drugs can also be used as antidepressant augmentation for nonresponders and partial responders.[38] The availability of extended-delivery preparations has reduced the risk of misuse of stimulants.[3, 38] Dexamphetamine produces pronounced stimulation of the CNS and increase motor activity, mental alertness and wakeness. It can also produce euphoria. Methylphenidate and modafinil are also included in this drug group.[3]

The most common forms of dementia are Alzheimer's disease and vascular dementia and mixed forms.[38] Cholinesterase inhibitors such as donepezil, galantamine and rivastigmine, are used in the treatment of mild and moderately severe dementia. They enhance cholinergic function in the central nervous system through reversible inhibition of acetylcholinesterase.[3, 38] Care should be taken when introducing these medications in patients with asthma, chronic obstructive airways disease, cardiac conduction abnormalities and peptic ulcers.[3]

Clonidine is used to control autonomic symptoms of opioid withdrawal and is used in the treatment of Tourette syndrome.[3, 38] Propranolol is used to treat the motor effects of antipsychotic-induced akathisia and prominent sympathetic symptom of acute anxiety disorder and social phobia (social anxiety disorder). It does not directly influence the psychic aspects of anxiety.[3]

2.3 The use of antipsychotic medication

Antipsychotic drugs play a central role in the treatment of most mental and behavioral disorders that require admission to hospital.[2, 57] Prescribing of antipsychotic drugs have vast diversity in terms of dose, indication, and combination with other psychotropic medications.[2, 46] Although the majority of experts and textbooks of psychiatry suggest monotherapy of psychotropics, psychopharmacology polypharmacy is considered to be essential in specific cases such as treatment for high level of agitation and danger to the patient himself or others and therapy resistance.[12, 46, 58]

2.3.1 Antipsychotic medication for treating psychiatric disorders

Antipsychotic medications are the cornerstone of treatment for psychotic illnesses. They are effective both for acute exacerbations and for long-term maintenance.[2, 3, 38]

Typical antipsychotics are more effective in treating positive than negative symptoms. Side effects of these drugs may mimic both positive and negative features of schizophrenia.[3, 5, 38] Their extrapyramidal side effects may not be differentiated with negative symptoms and the feature of akathisia can be similar with agitation and anxiety (positive symptoms). [38]

Standard practice for initial treatment of psychoses is using second generation antipsychotics or atypicals, such as risperidone, olanzapine, ziprasidone, aripiprazole, and quetiapine of which olanzapine and risperidone are the most frequently used.[2, 13] For chronic schizophrenia refractory and refractory atypical psychoses, olanzapine is more effective than other antipsychotics.[38] A benzodiazepine (e.g. lorazepam) is

added when agitation cannot be controlled. High potency first-generation antipsychotics (e.g., haloperidol) are reserved for nonresponders and partial responders with these two medications.[3, 38]

In treating bipolar disorder, antipsychotic drugs are used as mood stabilizers although psychosis symptoms are not present and patients have already used a mood stabilizer as prophylaxis. Antipsychotics are useful for acute mania, prophylaxis for preventing recurrent mania and bipolar depressive symptoms.[2, 13, 38]

The combination of an antipsychotics and antidepressants is more effective in treating depression with psychotic features than either class of drug alone. In addition, atypicals augment antidepressant drugs in treatment-resistent nonpsychotic depression.[38] Although some clinicians treat the most severe depressed patients with the older TCAs, the standard practice for this illness are combinations atypical drugs with newer antidepressants (e.g. SSRIs).[38]

The dosage of antipsychotics for depression with psychotic symptoms is usually slightly lower than the dosage used in acute psychoses. Patients may use an initial dosage that is equivalent to 4 to 6 mg of haloperidol per day or 5 to 10 mg per day olanzapine.[38]

Atypical antipsychotics offer some antidepressant effect and they can be used alone without antidepressants. In addition, they give less extrapyramidal side effects and tardive dyskinesia in which patients with mood disorder are more vulnerable.[38]

In treating patients diagnosed with drug induced psychosis, antipsychotics such as olanzapine and haloperidol are used to control psychotic or aggressive behavior with benzodiazepines for controlling agitation and anxiety.[33]

The antipsychotic drugs have been used in severe personality disorder (e.g., borderline) patients during periods of psychotic thinking and in treating and preventing episodes of impulsiveness, rage, and assaultiveness. Atypical antipsychotic drugs give more promising results.[35, 38]

2.3.2 Long-acting preparations of antipsychotic medications

The use of long-acting antipsychotic medications should be considered for patients who relapse because of noncompliance or the patients are unable to take oral medication.[3, 38] The depot preparations of fluphenezine decanoate, zuclopenthixol decanoate, haloperidol decanoate and risperidone decanoat are available in Australia.[3, 47]

The following guidelines are recommended when giving long-acting antipsychotics to get a safe and effective treatment. Before giving long-acting medication, a small dose is usually given orally to check adverse effects. The treatment starts with a low dose with oral supplementation to stabilize the treatment. The dose does not increase rapidly and to achieve a steady state plasma level may take 3 to 6 months (four to five dosing intervals). Symptoms of adverse effects should be monitored carefully to ensure the efficacy of treatment.[3, 38, 47]

Compared with oral risperidone, the use of long-acting risperidone reduces peak blood level around 30% and the plasma peak-to-trough ratio by 32 to 42%. These reductions may underline fewer adverse effects of long-acting risperidone than oral preparation. In addition, only 30% of patients who are treated with long-acting risperidon discontinued their treatment whereas almost 75% patients on oral discontinued their treatment. The reduction of discontinuation of treatment indicates that there is an improvement in patient adherence to the therapy. Switching from oral to long-acting risperidone produces an improvement in both symptoms and movement disorder.[59]

Shajahan et al[60] conducted a study comparing the effectiveness of long-acting risperidone with zuclopenthixol during a three year period (2002-2005). The results indicated that discontinuation due to adverse effect was less with risperidone than with zuclopenthizol (26% versus 63%, p=0.06). But both therapies are clinically effective in the longer treatment of psychotic disorder.

On the other hand, a study by Rubio et al[61] in chronic schizophrenia patients with substance use disorder showed that risperidone was more useful than zuclopenthizol

in reducing substance abuse and in alleviating symptoms of schizophrenia. Again the compliance of patients with risperidone was better than patients with zuclopenthizol.

2.3.3 As needed (pro renata= PRN) use of antipsychotic medications

Antipsychotic drugs given as pro renata use is a common practice in hospital. The purpose of administering antipsychotics this way is usually as acute treatment of psychotic symptoms or agitation. Giving pro renata antipsychotic drugs may indicate absence of a clear diagnosis or treatment strategy. [38, 62-64]

Patients receiving antipsychotic on an as-required basis are more likely to do poorly and they may be more likely to also be using an anti depressant on an as-needed basis. Moreover, in cases when patients are receiving only intermittent antipsychotic drug doses, physicians may get confused regarding the amount of antipsychotics that improves the psychotic disorder. [38, 62-64]

Using as-needed antipsychotics in longer term should be monitored because it may worsen the side effects or undiagnosed medical condition. [38]

2.3.4 Trends in the use of typical and atypical antipsychotic medications

The use of typical antipsychotic drugs has tended to decrease because of the side effects that are experienced by patients using this drug. On the other hand, there is an increasing trend in the use of atypicals.[5, 8, 9, 57]

The results of several clinical studies have shown that atypical antipsychotics are more effective in treating patients who are resistant to typical drugs, can control the negative and depressive symptoms of schizophrenia, and are associated with fewer extrapyramidal side effects. In addition, the use of atypicals to treat psychiatric patient reduces the length of stay in hospital.[1, 2, 5]

According to several studies in different countries, the increasing use of atypical antipsychotics has been followed by an increasing use of multiple antipsychotic drug regimens despite the lack of clinical and research data encouraging their use. In addition, an increased use of multiple antipsychotic drugs has been accompanied with increased doses of these drugs and the simultaneous use of other psychotropic drugs, such as antidepressants and mood stabilizers.[1, 65]

2.3.5 Monotherapy and polytherapy of antipsychotic medications

According to the current guidelines for treatment of psychotic disorders, atypical antipsychotic medications are first-choice therapy and the recommendation is to avoid polytherapy, especially combinations of atypical and typical antipsychotic drugs.[1, 58]

The results of surveys in the United States and several European countries revealed that psychiatric university clinics have a tendency to apply monotherapy to treat their patients with psychiatric illnesses but in psychiatric non-university clinics the use of monotherapy has decreased year by year.[46]

Also, in clinical practice, the use of a combination of atypical and typical antipsychotics to treat psychiatric patients, particularly in chronically ill psychotic patients, seems to be quite frequent and increasing. [1, 58, 66, 67] In a study conducted in Italy by Mauri et al[1] there was an increasing trend to use a combination of one typical and one atypical antipsychotic drug, and in the study conducted by Centorrino et al the combination of one typical and one atypical was the most common combination.[66] This tendency may reflect incomplete confidence in monotherapy with atypical antipsychotic agents.[66] In patients who typically show only limited benefits of treatment, the simultaneous use of more than one antipsychotic agent may reflect hopes for greater effectiveness of treatment involving drugs with somewhat dissimilar actions despite the lack of research evidence of superior effectiveness, a compromise of safety or an increase in the cost of care.[1, 66, 67]

Some countries such as Spain, Italy, Ireland, Germany, Denmark, England, Finland, Belgium, the Netherland and Norway do not accept drug combinations because

besides scant evidence that a combination of drugs is more effective than one-drug regimes; there is a greater risk of medication error in patients and also of serious cardiovascular and depressive side effects.[57]

There is some evidence that patients are treated with non-psychotropic drugs alongside psychotropics, which leads to patients being administered too many drugs. Polypharmacy in the treatment of psychiatric disorders is promoted by therapy strategies such as giving two drugs with a similar profile for one purpose, treating side effect by giving another drug instead of reducing the doses of the first, prescribing another different drug rather than increasing the dosage of the same one up to maximum, and starting a new treatment without stopping the ineffective one.[46, 58]

2.4 Factors influencing prescribing decision

There is a significant difference in the pattern of antipsychotic use in different places and the pattern is influenced by several factors. These factors are associated with both the characteristics of patients and physicians.

Factors that are associated with patient characteristics that have been found to affect psychotic treatment are sociodemographic characteristics such as age, sex, race, education, family status, employment and income as well as patients comorbidities such as the presence of a substance abuse disorder or comorbid depression with anxiety. [57, 68, 69] Patients' responses to psychotropic drug, their medical diagnosis, and expectations also impact on the prescribing of drug therapy.[57, 69]

Bowers et al. stated that genetic differences in European people could explain some differences in prescribing patterns across Europe. Antipsychotic and antidepressant are metabolized by a hepatic enzyme CYP2D6 whose activity is determined genetically.[57]

Diagnosis undoubtedly plays an essential role in drug therapy decisions and is the foundation from which the physician makes an appropriate decision.[69] Diagnosing

of psychiatric illnesses is more complicated than other disorders because mental disorders do not generally lend themselves to laboratory tests, physical measurements, and other means normally used to assist the physician in disease identification.[69] In addition, diagnosis does not always provide sufficient information to determine the appropriate or inappropriate use of psychotropic drugs.[69] Inadequate diagnostic information on medical records is likely to be the cause for some of the considerable off-label use and therapy differences.[68]

Some patients demand psychotropic drug therapy because they have become more willing to bring stressful life situation to the attention of their physician. [69, 70] Also more people consult doctors for their ailments and express their desire for drug therapy to the physician because health services are more available. [69, 70] According to this view, doctors are only passive distributors of drugs.[70] Once a doctor has prescribed psychotropic drugs and taught his patients an easy and acceptable way to handle their problems, perhaps on subsequent visits the patients may ask for these drugs again. Other patients may find out this approach of solving their disorder problems from relatives or friends who have same disorders or from other information sources such as the internet. [69, 70] The physician's treatment habits appear to affect patient expectations. [69, 70] The expectation of patients may be created by patients or physicians due to their treatment methods or by both of them.[69] However, Hadsall et al[69] who investigated factors affecting the prescribing of psychotropic and non-psychotropic drugs stated that there was a positive relationship between the expectations of drug therapy and non-psychotic drug prescribing. It reflected that doctors will prescribe drugs if the patients expect that drug therapy. This study indicated that the prescribing of psychotic drugs was much less predictable than that of non-psychotrop drugs. [69]

Factors such as physicians' attitude in prescribing, physicians' characteristics such as age, managed care involvement, being early adopters of new medical innovations, education and the experience of physicians also significantly influence prescribing patterns.[68, 69]

Prescribing characteristics of doctors are also affected positively by their colleagues as well as the closeness of working relationship with other physicians in group

practices.[69] Some doctors considered other physicians as the most important way to find out about new prescription drugs.[70] Doctors who had intensive contacts with a large number of their colleagues knew the new drug before their relatively isolated colleagues. However, the effect of other factors, such as advertising and education, were found to be greater than that of colleagues.[70]

Inexperienced physicians in the treatment of psychiatric problems are believed to assume that medication is the only way to treat the disorder and do not realize that other forms of treatment may also be effective.[69] In a study by Hadsall et al[69], board certified physicians tended to prescribe fewer psychotropic drugs for their patients than non-board certified physicians. In this case, among non-board certified physicians there was over-diagnosing of psychiatric problems.[69]

Basic therapeutic skills are provided and maintained by education and its success varies between countries and universities. The results of several studies indicated that education positively influences the quality of prescribing. Lower prescribing of drugs and higher appropriateness of therapy were associated with higher educational qualifications, being younger or having fewer years of professional experience but having more postgraduate training.[70]

Representatives of the drug industry argue that advertising helps doctor get up to date drug information but the contribution of advertising to prescribing is debatable. The purpose of advertising is to affect doctors' prescribing habits and to make them prescribe as many profitable preparations as possible. By communication and manipulation of opinions about drug therapy, advertising can create a new need and habits of drug consumption.[70]

A tighter control on the sales for special drugs, for example narcotics, has shown that drug consumption could be decreased by control measures, at least for short periods. The sale of drugs is also reduced after warnings of their side effects by the Adverse Drug Reaction Committee. Several studies showed that during the course of the studies the drug usage in hospital was notably decreased in some drug groups and the prescribing rates were very low. These studies suggested a positive effect of control measures if used effectively. [70]

2.5 The costs of treating psychiatric disorders

Psychiatric disorders have a major impact on the quality of life of patients and their families and significant cost implications.[71]

2.5.1 The categories of costs

Costs are divided into direct costs, indirect, and intangible costs.[20, 71-73] As the costs associated directly with a healthcare intervention, direct costs are categorized into direct medical and direct non-medical costs. [72] Direct medical costs include the costs of services and products used in the care of the patient, and may include expenditures for hospital stays, physician and other health professional visits, emergency department visits/services, home health care visits, laboratory tests, the cost of medications, and medical equipment and supplies.[20, 71-76] On the other hand, direct non-medical costs include the costs of non-medical assistance, food, accommodation, and transportation because of the illness or health care intervention.[72]

Indirect costs, which are also known as productivity costs, are the costs of lost or reduced productivity resulting from morbidity or premature mortality due to a medical condition or treatment. Intangible costs are the psychic costs associated with illness or treatment, such as anxiety, pain, depression, worry and other distress that patients and/or their families suffer. Because indirect and intangible costs are difficult or impossible to measure, most economic studies focus on costs from the perspective of the healthcare provider only. This mean that only direct medical costs are included.[71-73]

2.5.1.1 Cost of medications

The costs of psychotropic medications have a substantial contribution to mental health expenditure and vary from country to country.[68, 71] In developed countries, spending on medications accounts for between 1.1% and 10% of all direct health care costs.[10, 71, 76, 77] The growth rate per year of average annual spending on

psychotropic medications is faster than the growth rate for non-psychotropic medications.[68]

In 2001 in the United States, antipsychotic medications were the 13th-hightest drug category ranked by total retail sales.[68] The wider use and higher acquisition cost of atypical antipsychotic agents increases the share of the drug-costs in total costs. However, atypical drugs may prove cost effective if their efficacy reduces inpatient stays and results in fewer relapses, fewer inpatient admissions, and earlier discharge of patients from hospitals, which potentially reduces the total cost.[71]

2.5.1.2 Laboratory test costs

In the treatment of psychiatric patients, some laboratory tests are conducted to identify particular substances, monitor drug levels in urine and serum, and ascertain the side effect of medications. Significant expenses can be incurred with these tests.[33]

Investigating psychoactive substances is usually performed for patients with a current substance abuse disorder, especially alcohol or opioid use.[3] It is important to investigate the use of other substances, such as benzodiazepine, as multiple drug use is very common in this situation. Patients with mental disorders, particularly depression, psychoses, bipolar disorders, anxiety disorder (particularly social phobias), post-traumatic stress disorder (PTSD) and personality disorders, also often use substances such as alcohol, cannabis and amphetamines. [3, 38, 74]

Serum concentrations of drugs and their metabolites are a good indicator of both efficacy and toxicity. Therapeutic concentrations of medications, for example sodium valproate and carbamazepine, can be used as a general guide to the dosage of these drugs in bipolar disorder. Manic relapses in established bipolar disorder are often due to poor medication compliance, so serum concentrations should be checked.[3, 38] Serum concentration of drugs with a narrow therapeutic index such as lithium, should be carefully monitored for preventing the toxicity of the drug.[3]

Several laboratory tests are conducted for detecting the adverse effect of medications. The tests are performed prior to commencing the drugs and the tests are

usually repeated during the drug treatment and if there are any clinical features suggestive of adverse effects. For example, clozapine that is effective in treating refractory patients who are unresponsive to other drugs can cause agranulocytosis. Therefore, patients on clozapine require a weekly blood test to monitor their blood cell count.[3, 6, 28] Haematological, renal, electrolyte and hepatic functions should be assessed prior to commencing sodium valproate and carbamazepine. The haematological and hepatic function should be monitored at least each 3 to 6 months after treatment has been initiated.[3] For prevention of the development of neutropenia in mianserin use, a full blood count is conducted prior to use and during the treatment. Atypical antipsychotic medications influence cholesterol, lipid and glucose metabolism therefore fasting blood glucose and serum lipid estimations must be measured around the onset of treatment in all cases and annually thereafter to find out whether their level in the blood is above normal levels.[3, 30, 52]

2.5.1.3 Hospital inpatient bed day costs

Unit costs per bed day is a measure of hospital costs i.e., excluding drugs and diagnostic/laboratory tests and including other costs such as personnel, equipment and capital and food costs.[78]

The hospital inpatient bed day costs are the greatest contributor to the direct costs of admitted patients, and thus a reduction in hospital use would have an important impact on the overall costs of the illness. [79-81] The newer antipsychotic drugs have been found to reduce the length of hospital stays, the number of physician visits, and the overall cost of patient management.[28] Also, the longer patients received the newer antipsychotic medications, the fewer days they needed to remain hospitalized.[28]

2.5.2 Costs of treating mental disorders

Several studies have compared the costs of atypical and typical agents.[10, 82-85] These studies have suggested that atypical agents induce fewer extrapyramidal adverse effects than conventional drugs, improve patient compliance, and reduce the number of hospital admissions and hospital length of stay. As a consequence, despite the

increased acquisition costs, atypical agents appear no more expensive for health care system than typical agents.[82-84]

Hudson et al[10] reviewed the peer-reviewed literature of cost evaluations involving subjects with schizophrenia or a primary psychotic disorder that compared costs and benefits of the very expensive novel antipsychotics with those of the very inexpensive traditional antipsychotic medications. Several studies presented strong evidence for a cost advantage with atypical agents, while the others demonstrated a cost-neutral effect of the new generation antipsychotics and, in some cases, improved quality of life. In addition, 12 studies found that atypicals were equal or superior to typicals in terms of effectiveness.[10]

Rothbard et al assessed the utilization and cost of individuals with severe mental illness enrolled in Medicaid program in Florida, Oregon and Pennsylvania during 1997. The results of this study were that patients in the atypical only group had the highest cost for antipsychotics ($1798) and all pscyhotropics ($2174), and patients in the typical only group had the lowest ($291 and $578, respectively). Patients in the typical only group also had the lowest costs of inpatient services ($2140) and both pharmacy and psychiatric services ($3463). The group with the highest cost in these categories was in persons on combination typical/atypicals ($4200 and $6590, respectively).[86]

Rothbard et al also examined the difference in costs of atypical subgroups. Atypical combinations had the highest cost of antipsychotics ($2768) and all psychotropic ($3121), while risperidone had the lowest of those costs ($1249 and $1558, respectively) ($p<0.001$). Surprisingly, patients in the atypical combination group did not use inpatient services, and the olanzapine group had the highest hospital inpatient costs ($7873). As a result, the combined cost of medications and hospital care of the olanzapine group was the highest ($10231) and the atypical combination group was the lowest ($3712).[86]

Other studies[87, 88] comparing the costs of risperidone and olanzapine treatments showed similar results.[86] In a study conducted in Israel, Rabinowitz and colleagues examined differences in the total mental health care costs for one year following

initiation of risperidone or olanzapine in individual within an integrated managed mental health pilot project. The average daily retail price for risperidone was US$6.85 and for olanzapine was US$13.[85, 88] Johnsrud and colleagues who conducted a study to assess differences in the total mental health care costs for 1 year following initiation of risperidone or olanzapine in individual within an integrated managed mental health pilot project also found that antipsychotic medication costs were significantly lower for individuals prescribed risperidone than olanzapine ($1763 versus $2582; p<0.001).[87] Individuals prescribed risperidone had lower (but not significant) expenditures for inpatient mental health service ($3476 versus $3739; p=0.844), for mental health services that included outpatient and inpatient services, ($4714 versus 5077; p=0.792), and for total mental health care costs ($7407 versus $9011; p=0.255).[87]

However, not all studies have found olanzapine to result in lower costs. For example, cost data analysed for 48 olanzapine recipients and 43 risperidone recipients who completed 28 weeks' therapy found that although the drug acquisition costs for that period were higher in the olanzapine group ($US2278 per patient) than the risperidone group ($US2123 per patient), the total direct healthcare costs were lower for the olanzapine group than the risperidone group ($US5630 and $US6123 per patient, respectively). This represented a cost saving of $US493/patient for every 6 months that olanzapine was used instead of risperidone. This cost saving was due to saving in both out-patient and in-patients costs.[76]

Schizophrenia as the most common psychoses is probably the most expensive psychiatric disorder to treat.[76] Studies in England[75] and Italy[89] indicated that the care of patients with schizophrenia costs twice as much as the care of patients with other psychiatric disorders. This study also found that the mean costs for male patients were almost twice than that of female patients (€772.42 and €441.11 respectively).[89]

Percudani et al. also found that the cost of care for patients with schizophrenia was higher than for other patients with psychiatric illness. Their study identifying service utilization and the cost of first-contact patients in a community psychiatric services in Italy found that the average monthly costs per patient were €387 for patients with schizophrenia, €149 for mood disorders, €138 for neurotic and related disorders,

€129 for personality disorders, and €148 for other diagnoses. In-patient care of schizophrenia patients accounted for 74% of total costs, while it accounted for 56%, 25%, 31% and 25%, respectively, for the other groups.[90]

In another comparison of costs for patients with different types of psychiatric illness, patients with bipolar disease were found to have relatively high health care costs relative to those with depression.[84] Stensland et al[84] found that bipolar patients used significantly more psychiatric resources per person than patients with depression, and had more mean psychiatric hospital days, psychiatric and medical emergency room visits, and psychiatric office visits. Mean direct per-patient costs were $10,402 for bipolar patients and $7494 for depression patients ($p<0.001$), with the primary differences observed for psychiatric medication ($1641 vs. $507) and psychiatric hospitalization ($1187 vs. $241).[84]

2.6 Structure of dissertation

The literature reviewed in this chapter has illustrated many questions about the use of antipsychotic medications in the treatment of mental and behavioural disorders including the choice of drug regimens, patterns of prescribing, monotherapy versus polytherapy, and the cost of treating patients with mental illness. These issues are explored in this dissertation for a cohort of psychiatric patients admitted to the Armadale Kelmscott Memorial Hospital in 2005 who are prescribed antipsychotic agents.

The dissertation is structured as follows. Chapter 3 discusses the methodology for the study. Chapter 4 then presents the study results, and in Chapter 5 the findings of the study are discussed and interpreted in the context of the literature. Implications for future research are also addressed.

3 Methodology

The current study comprised two parts. The first part was a retrospective study of medical records of hospitalized psychiatric patients to retrieve demographic and clinical data. These data were used to identify the relationship between demographic and clinical features, evaluate the use of antipsychotic and other drugs, and identify factors relating to prescribing patterns of antipsychotic medications. The second part was collecting the cost of medications, laboratory tests and hospital inpatient bed day costs for conducting an economic analysis of the direct medical costs of treating these patients.

3.1 Ethical approval

The study involved the collection and analysis of patients' medical records. This required ethical approvals, which was obtained from both Curtin University of Technology Human Research Ethics Committee (HREC) (Appendix 1) and the Armadale Kelmscott Memorial Hospital (AKMH) HREC (Appendix 2). Both HRECs also provided a waiver of consent from patients for this study. The ethical issues arose as a result of the analysis of patient records and resultant issues in relation to confidentiality and the publication of data.

A unique non-patient identifiable code was allocated to each record to enable re-identification of the record if necessary. The key of the code was held at all time by the Manager of Pharmacy of AKMH. To ensure patients anonymity in the database, patient codes were kept separately during data entry and data analysis.

The data were kept in the School of Pharmacy, Curtin University of Technology during the study and will be stored in a locked archive for period of five years from the time of study and will be destroyed after that time. Only the investigators of the study are able to access the study records.

3.2 Study population

To be included in the study, patients were hospitalized at the Leshen Unit (Adult Psychiatry In-patient Unit), AKMH in 2005. Patients had to be at least 17 years of age and treated regularly with antipsychotic medications.

3.3 Data collection

The first step was to collect data from the medical records and the second step was obtaining the cost data.

3.3.1 Collection of the data from the medical records

Patient details obtained from the medical records included the date of birth, sex, date of admission, date of discharge, clinical details such as principle diagnosis, medications details including drug name, dose, frequency, route and number of dose administered, and length of therapy; laboratory tests related to monitoring of therapy and the treating psychiatrist team. Besides the data relating to psychotropic drugs such as typical and atypical antipsychotics; antidepressants (SSRI, TCA, MAOI), mood stabilisers (litium carbonate, carbamazepine, sodium valproate), anxiolytics and hypnotics (benzodiazepines, buspiron, zolpidem), anticholinergic drugs, and drugs used in alcohol and drug disorders (acamprosate, buprenorphine, methadone), non psychotropic medications were also collected. Non-psychotropc drugs that were included were anti-lipidemia (simvastatin, atorvastatin), antidiabetics (sulfonylureas, thiazolidinediones, metformin etc), antihypertensives (betablokers, ACE inhibitors, etc), antiinfectives (penicillins, macrolides, aminoglycosides, etc.), vitamins (single and multivitamin) and other drugs used to treat co-morbidities in psychiatric patients. These data were entered into Microsoft Excel sheets.

3.3.2 Collection of the cost data

Data on the unit costs of all medications (primary antipsychotic medications, adjunct and side-effect medications) was obtained from the Department of Pharmacy at the

AKMH. The unit costs of medication was based on the cost to public hospitals in Western Australia derived from the State Tender for Drugs, Disinfectants and Antiseptics, and Nutritional Products in 2005 (Contract No 5504).[91] Unit costs for laboratory tests were obtained from the Medicare Benefit Schedule, which was retrieved from the website of the Department of Health and Ageing.[92] Bed day costs excluding medications and laboratory tests was obtained from the Business Unit at the hospital. Inpatient bed day cost for psychiatric patients was AU $350 per day.

3.4 Data analysis

3.4.1 Data from the medical records

Statistical analysis of the data was performed using SPSS version 14 for Windows.

As continuous variables, age and duration of admission were assessed for normality, and natural logarithm transformations were applied for skewed data. In some instances where transformations did not achieve normality, non-parametric tests were used. Data relating to age and duration of admission were modified by collapsing these continuous variables into categorical variables.[93]

For the descriptive analysis, patients' ages were classified into five groups. These groups were less than 25, 25 to 34, 35 to 44, 45 to 54, and more than 54 years. Duration of admission (or length of stay) was also classified into five groups, namely 1 to 5, 6 to 10, 11 to 20, 21 to 40, and more than 40 days. Before doing statistical analysis, several categories were merged if the number of cases in each category did not meet with the assumptions of the method of analysis.[93, 94]

Diagnoses were coded based on the International Statistical Classification of Diseases and Related Health Problems, 10th Revision (ICD-10)[31] and were classified into six main diagnostic categories. These six main diagnoses were schizophrenia, bipolar affective disorders, depression, drug induced psychosis, personality disorders and miscellaneous. Diagnoses included in the miscellaneous category were psychiatric disorders that are not suitable with the criteria of the above mentioned five diagnoses. In the analysis of the patterns of antipsychotic use, this classification

was transformed into three categories, namely, schizophrenia, affective disorders (including bipolar affective disorder and depression), and miscellaneous (including drug induced psychosis, personality disorder and miscellaneous).

The prescribing patterns of antipsychotic medications were classified into three categories. These categories were typical, atypical, and combination typical- atypical antipsychotic drugs. Patients in the atypical group had at least one atypical antipsychotic during admission. Patients who were on at least one typical drug during their admission were included in the typical group. In the combination atypical-typical group, patients were treated with both atypical and typical drugs during their admission. If the patients were treated with more than one antipsychotic, these medications were not necessarily taken concurrently.

Descriptive statistical analyses were conducted on the data collected in the review of medical records. Frequency and percentage of patients according to age, gender, duration of admission, diagnosis, number of drugs and patterns of clinical use of antipsychotic medication were presented in tables or pie charts. Means, medians and standard deviations were also presented in these analyses, and the data were analyzed to determine the correlation between these demographic and clinical features, and also the patterns of clinical use of antipsychotic medications. Differences were tested using the chi-squared test.

Multinomial logistic regression analysis was conducted to identify factors affecting the prescribing of different antipsychotics to admitted psychiatric patients. Differences were considered statistically significant at $p<0.05$. Factors to be included in the regression included age, gender, duration of admission, diagnosis and the psychiatrist team.

3.4.2 Cost data

Total costs were calculated as the sum of medications, laboratory costs and bed day costs (excluding the cost of medications and laboratory costs). The cost data were used to calculate the costs of treating admitted psychiatric patients.

For the descriptive analysis, means were calculated for antipsychotics, psychotropics, all drugs, laboratory tests, bed days and total costs by demographic and clinical characteristic. These mean costs for patients who had used only atypival drugs (olanzapine, quetiapine, risperidone and combination atypical agents) were also calculated. Cost data were presented as means and standard deviations (rather than medians and interquartile ranges) despite being skewed. This is common practice in economic analysis as it allows total costs to be calculated. [95]

The distribution of the cost data of antipsychotics, psychotropics, all drugs, laboratory data, and total costs were assessed for normality. Natural logarithmic transformation was performed for normalizing the cost data. A one-way analysis of variance with post-hoc comparison was performed to determine which variables influenced the antipsychotic, psychotropic and total costs. The result of the post-hoc comparison shows where the differences of mean cost lies. Meanwhile the influence of gender and psychiatrist team toward these costs was analyzed with independent-samples t-test.

4 Results

The results of this study are presented in three sections. The first section shows the demographic and clinical features of hospitalized psychiatric patients on antipsychotic medication and the relationship between these characteristics. The second section shows the use of antipsychotic medications and other drugs prescribed for these patients and the factors that have a relationship with the prescribing patterns of antipsychotics. The last section is an economic analysis of the inpatient cost of treatment of psychiatric patients.

4.1 Research sample

In 2005, 381 patients were admitted to the Leshen Unit (Adults Psychiatry Inpatient Unit) AKMH. Medical records were available for review of 259 of these patients. Of the medical records that were reviewed, 182 cases received regular treatments of antipsychotic drugs. These 182 cases represented the research samples for this study.

4.2 Demographic characteristics

4.2.1 Age and gender

The number of patients on antipsychotic medications who were males (61%) was significantly more than the number of females (39%) (Chi-square=8.791, df = 1, p= 0.04) (Table 4.1).

More than three quarters of the patients were less than 45 years. The age group with the highest number of patients was the 35 to 44 year olds (30.8%), followed by the 25 to 34 year olds (23.6%) and the less than 25 year olds (22.5%). Overall, the mean age of admitted psychiatric patients was 35.9 ± 11.1 years.

Compared with the population of Armadale[96] aged 17 to 63 years in 2004, the percentages of patients aged less than 45 years (75%) was higher than population in those ages (55%). In the Armadale population, people aged more than 54 years had the highest proportion (25%) while people aged 35 to 44 and 45 to 54 year olds both accounted for 19% of population.

The age distribution of male and female patients was significantly different (chi-square=10.258 df=4, p=0.037). More female patients (33.8%) than male patients (16.2%) were 45 years or older, while more male than female patients were in the younger than 25 year age group (27.0% vs. 15.5%) and the 35 to 44 year age group (34.2 vs. 25.4%) (Table 4.1). The mean age of female and male patients were 38.3 ± 12.0 and 34.3 ± 10.3 years, respectively.

Table 4.1 Distribution of patients according to age and gender

Age Groups (years)	Gender				Total	
	Female		Male			
	N	%	N	%	n	%
<25	11	15.5	30	27.0	41	22.5
25-34	18	25.4	25	22.5	43	23.6
35-44	18	25.4	38	34.2	56	30.8
45-54	16	22.5	14	12.6	30	16.5
>54	8	11.3	4	3.6	12	6.6
Total	71		111		182	
%		39.0		61.0		100.0
Mean±SD	38.3±12.0		34.3±10.3		35.9±11.1	

4.3 Clinical Characteristics

4.3.1 Length of stay (LOS)

The length of stay of many patients on antipsychotic medications was less than 10 days (43.9%), with 21.4% being admitted for 5 or fewer days and 22.5% admitted for 6 to 10 days (Figure 4.1). Of the patients with longer hospital episodes, 26.9% were admitted for between 11 and 20 days and 18.7% and 10.4% respectively for 21 to 40 days and more than 40 days. Overall, the mean length of stay was 18.0 ± 18.3 days.

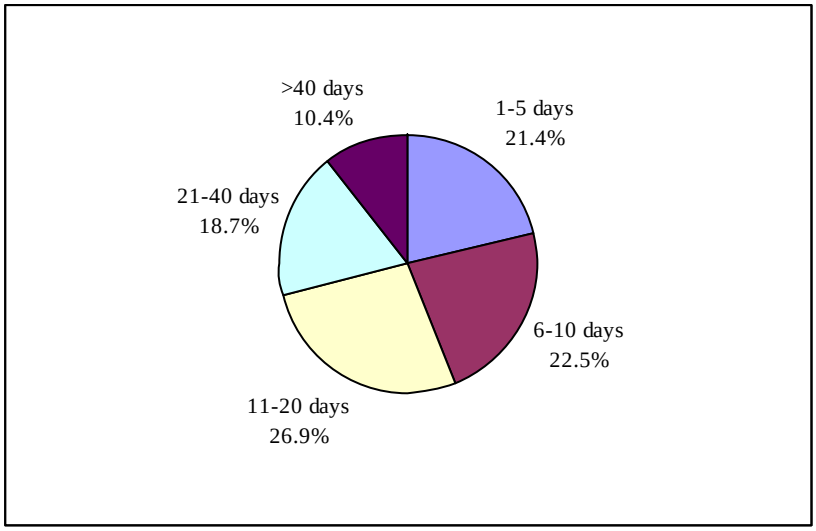

Figure 4. 1 Distribution of patients' length of stay

4.3.2 Diagnosis

Of the six diagnoses for mental illness, by far the most frequently occurring one amongst admitted psychiatric patients treated with antipsychotic medications was schizophrenia (40.7%) (Figure 4.2). Almost equal numbers of psychiatric patients were diagnosed as having bipolar effective disorder (17.0%) and drug induced psychosis (13.7%), while fewer were diagnosed with depression (11.0%), with personality disorders (9.9%) and with miscellaneous diagnoses (7.7%).

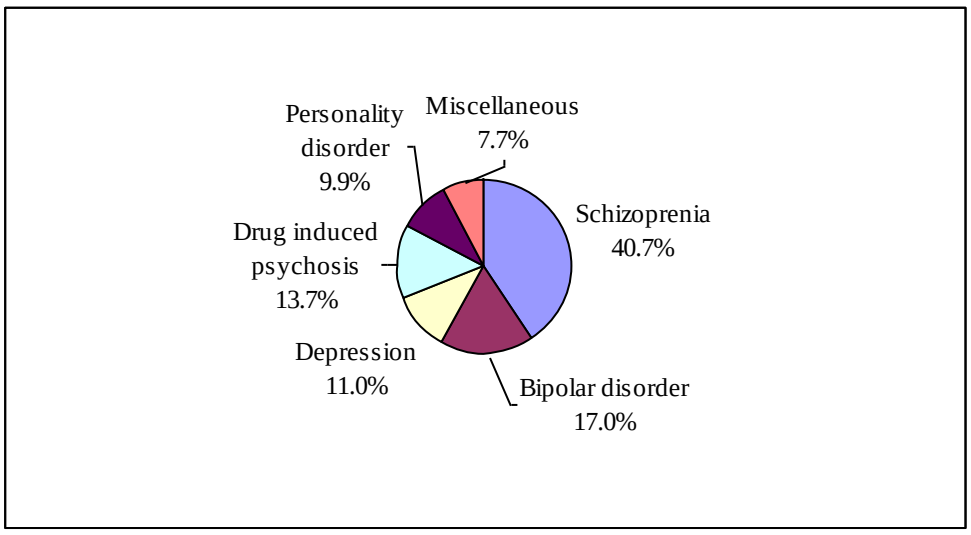

Figure 4.2 Distribution of patients by diagnosis

4.3.3 Psychiatrist team

There were two psychiatrist teams at the AKMH, i.e. team A and team B. Both team A and team B comprised a consultant psychiatrist, two registrars and two medical officers. Psychiatric patients whose home address was north of AKMH were treated by team A and those who lived south of the hospital were treated by team B.

The two psychiatrist teams treated almost an equal number of the admitted psychiatric patients with team A treating 56% of patients and team B treating 44% of patients (Chi-square=2.659, df=1, p=0.103).

4.4 Relationship between demographics and clinical characteristics

4.4.1 Length of stay and gender

The distribution of length of stay of male and female psychiatric patients was similar (Chi-square=2.316, df=4, p=0.680) (Table 4.2).

Table 4.2 Distribution of patients by length of stay and gender

LOS (days)	Gender				Total	
	Female		Male			
	n	%	N	%	n	%
1-5	18	25.4	21	18.9	39	21.4
6-10	18	25.4	23	20.7	41	22.5
11-20	16	22.5	33	29.7	49	26.9
21-40	12	16.9	22	19.8	34	18.7
>40	7	9.9	12	10.8	19	10.4
Total	71		111		182	100.0
%		39.0		61.0		100.0
Mean±SD	16.9±17.9		18.7±18. 7		18.0±18.3	
Abbreviation: LOS= length of stay						

4.4.2 Length of stay and age

The distribution of length of hospital admission for psychiatric patients of different ages was similar (Chi-square= 12.582, df=9, p=0.182) (Table 4.3). Older patients had a slightly longer hospital stay than younger patients, with the mean length of stay being 21 and 19 days for patients in the 35 to 44 and 45 and over year age groups and 17 and 14 for patients in the less than 25 and 25 to 34 year age group respectively.

Table 4.3 Distribution of patients by length of stay and age

LOS (days)	Age (years)								Total	
	<25		25-34		35-44		>44			
	n	%	N	%	N	%	n	%	n	%
1-5	9	22.0	16	37.2	8	14.3	6	14.3	39	21.4
6-10	11	26.8	7	16.3	13	23.2	10	23.8	41	22.5
11-20	9	22.0	13	30.2	15	26.8	12	28.6	49	26.9
>20	12	29.3	7	16.3	20	35.7	14	33.3	53	29.1
Total	41		43		56		42		182	
%		22.5		23.6		30.8		23.1		100.0
Mean±SD (days)	17.1±17.6		13.7±16.0		21.1±21.2		19.1±16.7			

Abbreviation: LOS= length of stay

4.4.3 Length of stay and diagnosis

Patients with different diagnoses had different patterns of length of stay (Chi-square= 45.472, df=9, p=0.000). The patients with schizophrenia and affective disorders had longer hospital stays than other patient (Table 4.4). While both schizophrenia and affective disorder patients had hospital length of stays of about 20 days, patients with drug induced psychosis had length of stays of around 10 days and patients with other disorders less than 10 days.

Table 4.4 Distribution of patients by diagnosis and length of stay

LOS (days)	Diagnosis								Total	
	Schizophrenia		Affective disorders*		Drug induced psychosis		Miscellaneous**			
	N	%	n	%	n	%	n	%	n	%
1-5	6	8.1	9	17.6	8	32.0	16	50.0	39	21.4
6-10	10	13.5	12	23.5	9	36.0	10	31.3	41	22.5
11-20	27	36.5	15	29.4	4	16.0	3	9.4	49	26.9
>20	31	41.9	15	29.4	4	16.0	3	9.4	53	29.1
Total	74		51		25		32		182	
%		40.7		28.0		13.7		17.6		100.0
Mean±SD	23.9±19. 5		19.7±20.9		10.0±8.3		8.0±8.7			

Abbreviation: LOS= length of stay
*Bipolar affective disorders and depression
**Personality disorders and other disorders

4.4.4 Length of stay and psychiatrist team

The length of stay of patients who were treated by psychiatrists in team A was longer than for patients who were treated by psychiatrists in team B (21.06 vs. 14.08) (Table 4.5). The percentage of patients treated in hospital for more than 40 days by psychiatrists in team A was considerable higher than for team B (16.7% vs. 2.5%). Meanwhile the percentage of patients treated in hospital for less than 40 days

Table 4.5 Distribution of patients by length of stay and psychiatrist team

LOS (days)	Psychiatrist team				Total	
	A		B			
	N	%	n	%	n	%
1-5	20	19.6	19	23.8	39	21.4
6-10	20	19.6	21	26.3	41	22.5
11-20	27	26.5	22	27.5	49	26.9
21-40	18	17.6	16	20.0	34	18.7
>40	17	16.7	2	2.5	19	10.4
Total	102		80		182	
%		56.0		44.0		100.0
Mean±SD	21.1±21.2		14.1±12.9			

Abbreviation: LOS= length of stay

by team B was considerably more for team A. As a result of these differences, the statistical analysis showed a statistically significant difference in the length of stay of patients who were treated by psychiatrist from team A compared with team B (Chi-square=10,007, df=4, p=0.040).

4.4.5 Diagnosis and gender

The number of males and females who suffered each psychiatric disorder was significantly different (Chi-square=16.585, df=5, p=0.004) (Table 4.6). The number of female patients who suffered depression, personality disorder and miscellaneous diagnoses (16.9%, 14.1% and 14.1 respectively) was more than for males. On the other hand, schizophrenia, bipolar disorder, and drug induced psychosis were diagnosed more in male than female patients. The most common psychiatric disorder in both female and male patients on antipsychotics was schizophrenia (29.6% and 47.7% respectively).

Table 4.6 Distribution of patients by diagnosis ad gender

Diagnosis	Gender				Total	
	Female		Male			
	n	%	n	%	n	%
Schizophrenia	21	29.6	53	47.7	74	40.7
Bipolar disorder	10	14.1	21	18.9	31	17.0
Depression	12	16.9	8	7.2	20	11.0
Drug induced psychosis	8	11.3	17	15.3	25	13.7
Personality disorder	10	14.1	8	7.2	18	9.9
Miscellaneous	10	14.1	4	3.6	14	7.7
Total	71		111		182	
%		39.0		61.0		100.0

4.4.6 Diagnosis and age

The proportion of patients suffering psychiatric disorders in each age category was significantly different (Chi-square=37.202, df=9, p=0.000) (Table 4.7). The most frequently occurring diagnosis for patients aged less than 25 year olds was

schizophrenia (28.4%). Meanwhile drug induced psychosis was the most frequently occurring diagnosis for patient aged 25 to 34 years; and affective disorders was the most common for patients aged more than 35 years.

Table 4.7 Distribution of patients by diagnosis and age

Age (years)	Diagnosis								Total	
	Schizophrenia		Affective disorders*		Drug induced psychosis		Miscellaneous**			
	n	%	n	%	n	%	N	%	n	%
<25	21	28.4	6	11.8	5	20.0	9	28.1	41	22.5
25-34	16	21.6	6.0	11.8	15	60.0	6.0	18.8	43	23.6
35-44	24	32.4	18	35.3	5	20.0	9	28.1	56	30.8
>44	13	17.6	21	41.2	0	0.0	8	25.0	42	23.1
Total	74		51		25		32		182	
%		40.7		28.0		13.7		17.6		100.0
Mean±SD	34.2±10.1		41.7±11.6		29.4±6.2		35.7±11.7			

*Bipolar affective disorders and depression
**Personality disorders and other disorders

Patients with drug induced psychosis had the lowest mean age (29.4 years); in contrast patients with affective disorders were the oldest (41.7 years). The age of patients with other disorders was similar at approximately 35 years.

4.4.7 Diagnosis and psychiatric team

The pattern of diagnoses of the patients who were treated by psychiatrist team A and psychiatrist team B was not statistically significantly different (Chi-square=8.433, df=5, p=0.139), although differences did exist. Forty eight percent of patients who were treated by team A were diagnosed with schizophrenia while less than one third of patients treated by team B were diagnosed with this disorder. The percentage of patients with bipolar disorder, depression, drug induced psychosis, and personality disorder in team A was significantly less than those in team B (11.8% vs. 23.8%, 10.8% vs. 11.3%, 12.7% vs. 15% and 7.8% vs. 12.5% respectively). On the other hand, team A took care of patients with miscellaneous diagnosis more than team B (8.8% vs.6.3%). (Table 4.8)

Table 4.8 Distribution of patients by diagnosis and psychiatrist team

Diagnosis	Psychiatrist team				Total	
	A		B			
	N	%	n	%	n	%
Schizoprenia	49	48.0	25	31.3	74	40.7
Bipolar disorder	12	11.8	19	23.8	31	17.0
Depression	11	10.8	9	11.3	20	11.0
Drug induced psychosis	13	12.7	12	15.0	25	13.7
Personality disorder	8	7.8	10	12.5	18	9.9
Miscellaneous	9	8.8	5	6.3	14	7.7
Total	102	100.0	80	100.0	182	100.0
% treated		56.0		44.0		100.0

4.5 Pattern of use of psychotropic and other medications for treating psychiatric patients

Table 4.9 and Table 4.10 show drugs that were used by psychiatric inpatients in this study. Table 4.9 includes only drugs that were used as regular treatments, while Table 4.10 includes use of regular treatments as well as ‘as needed” or pro re nata (PRN*)* medications.

4.5.1 Pattern of drugs as regular treatments

4.5.1.1 Pattern of antipsychotic medications as regular treatment

Antipsychotic medications were the most often drug used for treating the patients, accounting for around 35% of the drugs used. Of these drugs, 32.9% was atypical antipsychotic drugs and only 2.9% were typicals.

Olanzapine was the atypical antipsychotic that was most often used as routine antipsychotics with 91 patients treated with this drug; followed by quetiapine and risperidone (52 and 46 cases respectively). Typical drugs that were the most frequently used were chlorpromazine (six patients), trifluorperazine (four patients), zuclopenthixol (three patients) and haloperidol (three patients).

Combinations of quetiapine-olanzapine (10 cases) and risperidone-olanzapine (10 cases) were the most common combinations of two atypicals. The combination of quetiapine with risperidone and amilsulpride with clozapine were found in five cases and four cases respectively. Antipsychotic polytherapy with three atypicals most generally used a combination of quetiapine-risperidone-olanzapin and quetiapine-olanzapine-clozapine, each these combinations being used for two cases.

Chlorpromazine (two cases) and trifluorperazine (two cases) were the typical antipsychotics that were most common used as regular typical monotherapy. These drugs and other typicals, such as, zuclopenthixol decanoate, haloperidol, pimozide and pericyazine were also used as monotherapy and polytherapy antipsychotics by combining with other atypical or typical medications.

Table 4.9 Antipsychotic and other medications for treating hospitalized psychiatric patients in 2005 as regular use

Type of drug		The most commonly used drugs*					
	%	Drug 1	n	Drug 2	N	Drug 3	n
Atypical Antipsychotics	32.6	Olanzapine	91	Quetiapine	52	Risperidone	46
Typical antipsychotics	2.9	Chlorpromazine	6	Triflourperazine	4	Zuclopenthixol	3
Anxiolytics & hipnotics	19.0	Temazepam	40	Lorazepam	33	Clonazepam	22
Antidepressant	9.2	Mirtazepin	17	Venlafaxine	8	Sertraline	8
Mood stabilizers	10.1	Sodium valproate	42	Lithium carbonate	9	Carbamazepine	7
Anticholinergics	1.6	Benztropine	11	-		-	
Analgesics	2.2	Ibuprofen	5	Paracetamol	2	Panadeine	2
Gastrointestinal drugs	3.7	Esomeprazole	4	Omeprazole	4	Loperamide	3
Vitamins	4.8	Thiamine	12	Multivitamin	9	Folic acid	4
Cardiovascular drugs	3.8	Simvastatin	9	Propanolol	8	Atorvastatin	3
Respiratory drugs	1.9	Fluticasone	8	Salbutamol SO4	3	Ipratropium	2
Antibacterials	2.6	Amoxicillin	8	Trimethorpin	2	Flucloxacillin	2
Others	5.3	Metformin	6	Nystatin	4	FeSO4	4
Total	100.0						

* Patients could receive more than one medication.

4.5.1.2 Patterns of other medications as regular use

In regular treatment, anxiolytic and hypnotic medications were the second type of drugs that were most often used (19%). In this class of drugs, temazepam (40 cases) was the most frequent used, followed by, lorazepam (33 cases), clonazepam (22 cases), diazepam (nine cases) and nitrazepam (six cases).

Antidepressants accounted for around 9.2% of the drugs. The most often antidepressant used was mirtazepine (17 patients); with venlafaxine and sertraline used by eight patients. Other antidepressants such as fluoxetine, citalopram, clomipramine, escitalopram oxalate, and mianserin were used less frequently than those three drugs. Meanwhile, sodium valproate (42 patients) was the most frequent mood stabilizer used, followed by lithium carbonate (nine patients), and carbamazepine (seven patients).

Anticholinergic medication for treating extrapyramidal side effect accounted for 1.5% of drugs used with only benztropine used regularly (11 patients).

Non psychotropic medications are drugs for treating comorbidities. Including in this group are gastrointestinal drugs, cardiovascular drugs, respiratory drugs, analgesics, vitamins, antibacterials, cardiovascular drugs, antidiabetics etc. These drugs accounted for 24.3% of all drug used by the patients.

4.5.2 Pattern of psychotropic drugs as regular treatments and PRN medications

Table 4.10 shows the drugs for psychiatric patients in this study including drugs that were given to the patients when they needed those drugs (PRN use). Psychotropics that were sometimes given as PRN drugs were antipsychotic, anxiolytic and hypnotic and anticholinergic medications, while non-psychotropic drugs that were usually used as needed drugs were analgesics and salbutamol inhalers.

4.5.2.1 Patterns of antipsychotic medications as regular and as PRN use

Atypical antipsychotic agents most commonly prescribed as PRN use were olanzapine and quetiapine. These two drugs were prescribed as PRN for 12 cases. In the typical group, chlorpromazine was the most frequently prescribed drug for PRN , with it being used for 21 cases. Four patients also were treated with droperidol as PRN use.

The patterns of antipsychotic use were changed when PRN use was included in the overall analysis. Olanzapine, quetiapine and risperidone were still the three most often monotherapy atypicals for treating patients. One hundred and three patients used olanzapine; 64 and 46 patients were treated with quetiapine and risperidon respectively. Chlorpromazine as typical monotherapy was used in 27 patients.

Olanzapine was the most frequently used in combinations of two atypicals. It was combined with quetiapine in 15 patients, with five of these patients getting quetiapine as PRN drugs. Olanzapine was combined with with risperidone for treating 15 patients and olanzapine was given as needed drug for seven of those patients.

Besides olanzapine, quetiapine was also used as two atypicals with other antipsychotics. Eight patients were treated with quetiapine-risperidone and three of them got quetiapine as PRN drug. Two of four patients on a combination of aripiprazole and quetiapine also got a PRN quetiapine.

Olanzapine was the most often antipsychotic combining with more than two other antipsychotics. Olanzapine with quetiapine and chlorpromazine was used for five patients with three of these patients getting chlorpromazine as a PRN drug. There was also a combination of olanzapine with quetiapine and risperidone, with chlorpromazine and droperidol, amisulpride and chlorpromazine, and with quetiapine and zuclopenthixol.

Chlorpromazine as typical antipsychotics was frequently used as a PRN drug and combined with other antipsychotics. Only one case was on olanzapine and chlorpromazine as a regular drug but chlorpromazine as PRN drug combined with olanzapine was used in five cases. Chlorpromazine as PRN drug also was combined with amilsulpride (four cases), risperidone (three cases) and quetiapine (one case). Chlorpromazine was used with two or more antipsychotics usually also as a PRN drug.

A few patients in this study got droperidol as PRN use. Four patients used this drug, either in a combination of droperidol with olanzapin and chlorpromazine (three patients) or risperidone and chlorpromazine (one patient). Chlorpromazine used by those patients was also as PRN drug.

Other typicals, such as haloperidol, zuclopenthixol decanoate, triflouperazine, pericyazine, and pimozide were regular drugs. They usually were combined with other antispychotics. Zuclopenthixol decanoate and droperidol were an intra muscular injection.

4.5.2.2 Patterns of other medications as regular and as PRN use

The number of patients receiving anxiolytic and hypnotic drugs as PRN prescription were extremely high. The number of patients getting lorazepam (58 patients) and clonazepam (44 patients) as PRN medications was approximately twice the number cases using these drugs as routine prescriptions (33 and 22 patients, respectively). The number of patients treated regularly with temazepam was similar with those with PRN use (around 40 patients).

The use of anticholinergic medication as PRN medication was also high, with 19 patients in this category.

Table 4.10 Psychotropic and other medications for treating hospitalized psychiatric patients in 2005 as regular and PRN use

Type of drug		The most commonly used drugs*					
	%	Drug 1	n	Drug 2	n	Drug 3	n
Atypical Antipsychotics	27.3	Olanzapine**	103	Quetiapine**	64	Risperidone	46
Typical antipsychotics	4.8	Chlorpromazine**	27	Triflouperazine	4	Droperidol**	4
Anxiolytics & hipnotics	29.3	Temazepam **	79	Lorazepam **	91	Clonazepam**	66
Antidepressant	6.5	Mirtazepin	17	Venlafaxine	8	Sertraline	8
Mood stabilizers	6.6	Sodium valproate	42	Litrium carbonate	9	Carbamazepine	7
Anticholinergics	2.2	Benztropine**	20	-		-	
Analgesics	4.0	Paracetamol**	14	Panadeine**	10	Ibuprofen**	6
Gastrointestinal drugs	3.5	Esomeprazole	4	Omeprazole	4	Loperamide	3
Vitamins	3.5	Thiamine	12	Multivitamin	9	Folic acid	4
Cardiovascular drugs	3.1	Simvastatin	9	Propranolol	8	Atorvastatin	3
Respiratory drugs	2.7	Salbutamol SO4**	13	Fluticasone	8	Beclomethasone	2
Antibacterials	2.0	Amoxicillin	8	Trimethoprin	2	Flucloxacillin	2
Others	5.3	Metformin	6	Nystatin	4	FeSO4	4
Total	100						
* Patients could receive more than one medication.							
** including regular and PRN (as needed) uses							

Non anti psychotropic drugs that were used as PRN drugs in this study were analgesics, such as paracetamol, panadeine and ibuprofen and salbutamol sulphate inhaler. There were 13 patient treated with paracetamol as needed drug, eight patients with panadeine, one patient with ibuprofen and 10 patients with salbutamol sulphate inhaler.

4.6 Association between patterns of use of antipsychotic medications and patients' characteristics.

Chi-squared tests and multinomial logistic analyses were conducted to examine whether there was a significant association between patterns of antipsychotic use and demographic and clinical characteristics. The patterns of antipsychotic use were classified into five group and categories of age, length of stay and diagnoses were transformed into three categories in order to meet with chi-square assumption, in which no more than 20% of the cells have expected frequency less than five.[94, 97]

4.6.1 Patterns of antipsychotic use excluding PRN antipsychotics

The classification of antipsychotic medication use in Table 4.11 was based on the antipsychotics that were used as regular medications. The patterns of use of antipsychotic medications did not differ significantly between male and females, age, length of stay categories and psychiatrist teams.

The only statistically significant difference in the pattern of use of antipsychotic medications was for diagnosis (p=0.001). The main difference was found between schizophrenia and the other diagnoses. Patients with schizophrenia were treated relatively more frequently with risperidone, combination atypicals and other monotherapy atypicals than patients with affective disorder and miscellaneous disorders. On the other hand, patients with affective disorder and miscellaneous disorders were treated relatively more frequently with olanzapine and quetiapine.

Table 4.11 Distribution of patients' characteristics by antipsychotic use (excluding PRN antipsychotics)

Characteristics		Antipsyhotic medications														Total			
		Olanzapine		Quetiapine		Risperidone		Combination atypical		Other monotherapy atypical		Typicals		Combination typical-atypical				Chi-square*	p-value*
		N	%	n	%	n	%	N	%	N	%	n	%	n	%	n	%		
Gender	Female	22	31.0	13	18.3	10	14.1	14	19.7	5	7.0	4	5.6	3	4.2	71	39.0	4.704	0.327
	Male	38	34.2	9	8.1	14	12.6	28	25.2	12	10.8	4	3.6	6	5.4	111	61.0		
Age (years)	<35	26	31.0	6	7.1	13	15.5	21	25.0	10	11.9	2	2.4	6	7.1	84	46.2	6.172	0.635
	35-44	17	30.4	10	17.9	7	12.5	12	21.4	5	8.9	3	5.4	2	3.6	56	30.8		
	>44	17	40.5	6	14.3	4	9.5	9	21.4	2	4.8	3	7.1	1	2.4	42	23.1		
	Mean±SD	37.17±11.39		38.09±9.75		33.54±10.60		35.19±11.60		32.29±9.58		41.13±12.81		33.22±11.8					
LOS (days)	1-5	10	25.6	8	20.5	5	12.8	6	15.4	5	12.8	2	5.1	3	7.7	39	21.4	10.350	0.242
	6-10	17	41.5	4	9.8	2	4.9	10	24.4	3	7.3	4	9.8	1	2.4	41	22.5		
	>10	33	32.4	10	9.8	17	16.7	26	25.5	9	8.8	2	2.0	5	4.9	102	56.0		
	Mean±SD	14.83±12.43		18.0±19.24		25.42±23.44		22.29±23.84		14.12±10.95		8.25±6.43		15.11±15.71					
Diagnosis	Schizophrenia	16	21.6	2	2.7	15	20.3	26	35.1	11	14.9	1	1.4	3	4.1	74	40.7	27.813	0.001
	Affective disorder**	22	43.1	10	19.6	4	7.8	8	15.7	2	3.9	3	5.9	2	3.9	51	28.0		
	Miscellaneous***	22	38.6	10	17.5	5	8.8	8	14.0	4	7.0	4	7.0	4	7.0	57	31.3		
Psychiatrist Team	A	30	29.4	13	12.7	18	17.6	27	26.5	7	6.9	3	2.9	4	3.9	102	56.0	8.682	0.67
	B	30	37.5	9	11.3	6	7.5	15	18.8	10	12.5	5	6.3	5	6.3	80	44.0		
	Total	60		22		24		42		17		8		9		182			
	%		33.0		12.1		13.2		23.1		9.3		4.4		4.9		100.0		

LOS= length of stay

*other monotherapy atypical, typical and combination of typical-atypical were combined to meet the assumptions of chi-square test

** bipolar affective disorders, depression

*** drug induced psychosis, personality disorder, other disorders

4.6.2 Patterns of antipsychotic use including PRN antipsychotics

Several patients got olanzapine, quetiapine, chlorpromazine or droperidol as PRN drugs; which changed the number of patients treated with each of the antipsychotic categories (Table 4.12). The number of patients on atypical monotherapy and typicals monotherapy decreased while the number of patients on combination atypical and combination atypical-typical increased.

The patterns of use of antipsychotic medications did not differ significantly by gender, age or length of stay categories, but did differ significantly by diagnosis and treatment team.

A statistically significant association was found between the pattern of antipsychotic medications and diagnosis. Patients with schizophrenia were most commonly treated with a combination of atypicals (44.6%), with the next most common treatment being olanzapine (16.2%). Patients with affective disorders and miscellaneous diagnoses were most commonly treated with olanzapine (33.3% and 29.8% respectively) followed by a combination of atypicals (19.6% and 19.3% respectivey) and quetiapine (15.7% and 15.8% respectively).

When PRN antipsychotic use was also included in the classification of antipsychotic use, there was a highly statistically significant association between the patterns of use and psychiatrist team ($p<0.001$). Team A prescribed relatively more combination atypicals and fewer combination atypical-typicals than Team B. Furthermore, no cases treated by Team B were treated with risperidone.

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Table 4.12 Distribution of patients' characteristics by antipsychotic use (including prn antipsychotics)

Characteristics		Antipsychotic medications														Total			
		Olanzapine		Quetiapine		Risperidone		Combination atypicals		Other atypical monotherapy		Typicals		Combination atypical typical				Chi-square*	p-value*
		n	%	N	%	n	%	n	%	N	%	N	%	n	%	n	%		
Gender	Female	18	25.4	11	15.5	5	7.0	20	28.2	5	7.0	3	4.2	9	12.7	71	39	3.663	0.453
	Male	28	25.2	8	7.2	7	6.3	34	30.6	8	7.2	4	3.6	22	19.8	111	61		
Age (years)	<35	19	22.6	5	6.0	6	7.1	28	33.3	8	9.5	2	2.4	16	19.0	84	46	7.924	0.444
	35-44	13	23.2	10	17.9	3	5.4	14	25.0	4	7.1	3	5.4	9	16.1	56	31		
	>44	14	33.3	4	9.5	3	7.1	12	28.6	1	2.4	2	4.8	6	14.3	42	23		
	Mean±SD	38.04±11.44		37.32±9.89		36.42±11.07		34.2±11.94		32.23±9.471		38.0±10.02		35.48±10.78					
LOS (days)	1-5	7	17.9	7	17.9	3	7.7	9	23.1	3	7.7	1	2.6	9	23.1	39	21	9.881	0.276
	6-10	14	34.1	3	7.3	0	0.0	14	34.1	2	4.9	4	9.8	4	9.8	41	23		
	>10	25	24.5	9	8.8	9	8.8	31	30.4	8	7.8	2	2.0	18	17.6	102	56		
	Mean±SD	15.43±13.45		18.95±20.33		32.42±29.11		17.59±16.85		16.69±11.03		9.14±6.39		18.84±22.9					
Diagnosis	Schizophrenia	12	16.2	2	2.7	7	9.5	33	44.6	9	12.2	1	1.4	10	13.5	74	41	23.35	0.003
	Affective disorder**	17	33.3	8	15.7	1	2.0	10	19.6	2	3.9	2	3.9	11	21.6	51	28		
	Miscellaneous***	17	29.8	9	15.8	4	7.0	11	19.3	2	3.5	4	7.0	10	17.5	57	31		
Psychiatrist Team	A	27	26.5	12	11.8	12	11.8	33	32.4	5	4.9	2	2.0	11	10.8	102	56	19.41	<0.001
	B	19	23.8	7	8.8	0	0.0	21	26.3	8	10.0	5	6.3	20	25.0	80	44		
	Total	46	25.3	19	10.4	12	6.6	54	29.7	13	7.1	7	3.8	31	17.0	182	100		
	%		25.3		10.4		6.6		29.7		7.1		3.8		17.0		100		

LOS= length of stay

*other monotherapy atypical, typical and combination of typical-atypical were combined to meet the assumptions of chi-square test

** bipolar affective disorders, depression

*** drug induced psychosis, personality disorder, other disorders

4.6.3 Factors associated with the patterns of antipsychotic medication use

Multinomial logistic regression analysis was conducted to further investigation the factors associated with patterns of antipsychotic use.

4.6.3.1 Factors associated with the patterns of antipsychotic use (excluding PRN use)

The results of the multinomial logistic regression are presented in Table 4.13 and Table 4.14. The results of the likelihood ratio tests (Table 4.13) indicated that diagnosis was the only factor associated with antipsychotic use if the classification of antipsychotic use patterns excluded the PRN antipsychotics. The output further suggested that the odds were statistically significantly higher that schizophrenic patients versus patients with miscellaneous diagnosis would be treated with risperidone rather than olanzapine (4.348; 95% CI 1.083-17.463) (Table 4.14) and with combination atypicals than olanzapine (5.388; 95% CI 1.680-17.277).

Table 4.13 Likelihood Ratio Tests

Characteristic/Variable	-2 Log Likelihood Reduced	Chi-Square	Df	p
Gender	338.899	3.533	4	0.473
Age (years)	341.858	6.492	8	0.592
LOS (days)	343.648	8.283	8	0.406
Diagnosis	359.017	23.651	8	0.003
Psychiatrist team	342.725	7.359	4	0.118

Table 4.14 Multinomial logistic regression analysis of patterns of antipsychotic use (excluding PRN antipsychotics)

Antipsychotic	Characteristic/ Variable	P	Odds Ratio	95% Confidence Interval
Risperidone	Diagnosis:			
	Schizophrenia	0.038	4.349	1.083-17.463
	Affective disorders	0.908	1.097	0.225-5.346
	Miscellaneous*	-	-	-
Combination atypical	Diagnosis:			
	Schizophrenia	0.005	5.388	1.680-17.277
	Affective disorders	0.678	1.302	0.374-4.534
	Miscellaneous*	-		
Olanzapine is the reference category of antipsychotic pattern * drug induced psychosis, personality disorder, miscellaneous				

4.6.3.2 Factor associated with the patterns of antipsychotic use (including PRN use)

Tables 4.15 and 4.16 repeat the above analyses including PRN use of antipsychotics. Table 4.15 confirms a statistically significant association between both diagnosis and psychiatrist team and the pattern of antipsychotic use. The odds were 6.178 (95% CI 1.927-19.807) times higher of treating with combination atypical over olanzapine if the diagnosis was schizophrenia versus miscellaneous diagnoses (Table 4.16). The odds of choosing olanzapine versus miscellaneous antipsychotics by psychiatrist team B was 2.915 (CI 1.228-6.896) higher than the odds for team A.

Table 4.15 Likelihood Ratio Tests

Characteristic/Variable	-2 Log Likelihood Reduced	Chi-Square	df	p
Gender	308.003	2.771	4	0.597
Age (years)	314.766	9.534	8	0.299
LOS (days)	317.726	12.493	8	0.130
Diagnosis	329.348	24.116	8	0.002
Psychiatrist team	328.502	23.269	4	0.0001

Table 4.16 Multinomial logistic regression analysis of patterns of antipsychotic use pattern (including PRN antipsychotics)

Antipsychotic	Characteristic/ Variable	p	Odds Ratio	95% Confidence Interval
Combination atypical	Diagnosis:			
	Schizophrenia	0.002	6.178	1.927-19.807
	Affective disorders	0.750	1.216	0.366-4.043
	Miscellaneous*	-		
Miscellaneous**	Psychiatrist team			
	B	0.015	2.915	1.228-6.896
	A	-		

Olanzapine is the reference category of antipsychotic pattern
* drug induced psychosis, personality disorder, miscellaneous
** other monotherapy atypical, typical, combination atypical-typical

4.7 Economic analysis

The cost of drugs was calculated using both drugs as regular and PRN use in the economic analysis.

4.7.1 Total mean costs by cost category

Several factors influenced the cost of treating patients (Table 4.17). In terms of total cost, the mean cost of treating male patients was higher than female patients and patients in the 35 to 44 year age group had a higher mean cost than patients in other age groups. Increasing the length of stay caused the mean cost to increase. Patients with schizophrenia had a higher mean cost than patients with other diagnoses, while patients who were treated by psychiatrist team A had a higher mean cost than those treated by team B. If patients are grouped by antipsychotic use, patients on combination atypicals had the highest mean cost.

The cost of individual cost categories was also investigated. In general, the differences in total cost by demographic, clinical and treatment factors discussed above were maintained for the different cost categories but with some interesting findings. The mean cost of antipsychotic medications varied considerably across

patients based on treatment group. The mean cost of patients on combination atypicals was $174.39 compared with $73.07 for patients on risperidon oral and

Table 4.17 Distribution of mean cost amongst demographic and clinical characteristics

Characteristics		Mean Cost (A$)					
		Antipsy-chotics	Psycho-tropics	All drugs	Laboratory tests	Bed days	Total
Gender							
Male	Mean	162.04	181.56	191.99	152.54	6545.95	7234.07
	SD	208.62	234.08	251.40	99.75	6535.74	7150.28
Female	Mean	92.30	107.47	117.96	145.57	5905.63	6368.93
	SD	130.34	138.00	147.87	94.55	6247.54	6521.45
Age (years)							
<35	Mean	129.13	142.00	147.59	141.35	5379.17	5939.24
	SD	192.92	207.29	213.61	98.60	5872.92	6427.29
35-44	Mean	158.79	185.33	198.73	145.45	7387.50	8075.80
	SD	203.34	239.64	265.66	102.05	7434.12	8014.92
>44	Mean	114.29	130.40	146.65	172.59	6675.00	7238.94
	SD	137.18	138.16	152.09	87.49	5849.67	6072.16
LOS (days)							
1-5	Mean	19.83	22.90	26.41	104.25	1023.08	1196.47
	SD	15.08	16.91	21.40	74.17	470.84	499.61
6-10	Mean	58.76	66.95	72.51	147.20	2774.39	3119.81
	SD	56.90	59.21	60.70	76.98	465.58	537.01
>10	Mean	209.38	236.72	251.79	168.30	9727.94	10594.14
	SD	216.38	238.98	257.32	107.18	6776.08	7288.83
Diagnosis							
Schizophrenia	Mean	207.82	225.25	232.92	155.55	8347.97	9169.50
	SD	217.44	235.75	241.78	107.44	6807.41	7301.52
Affective disorders	Mean	129.64	159.02	181.14	160.03	6876.47	7506.30
	SD	183.89	217.65	253.06	95.76	7298.76	7866.85
Others	Mean	44.72	52.73	56.35	133.26	3113.16	3400.21
	SD	57.68	61.39	63.22	84.29	2976.24	3131.54
Psychiatrist team							
A	Mean	140.42	163.00	177.16	144.42	7370.59	7995.59
	SD	183.69	209.82	228.39	100.13	7421.00	7933.16
B	Mean	127.70	139.47	145.19	156.71	4926.25	5495.33
	SD	187.31	198.94	207.63	94.33	4526.52	5027.34

Table 4.17 Distribution of mean cost amongst demographic and clinical characteristics (continued)

Characteristics		Mean Cost (A$)					
		Antipsy-chotics	Psycho-tropics	All drugs	Laboratory tests	Bed days	Total
Antipsychotic medications							
Olanzapine	Mean	93.10	112.02	120.79	157.07	5402.17	5885.16
	SD	98.89	113.25	118.31	73.01	4708.28	4911.60
Quetiapine	Mean	103.12	126.98	140.63	172.31	6631.58	7174.63
	SD	159.19	188.99	209.48	107.78	7117.12	7744.42
Risperidone*	Mean	96.56	106.29	106.63	133.57	10446.15	10889.21
	SD	116.71	118.67	118.45	100.08	9475.72	9813.66
Combination	Mean	174.39	191.82	202.17	138.18	6008.33	6714.89
Atypicals	SD	213.26	231.83	240.90	97.19	5796.62	6346.08
Others**	Mean	152.50	169.56	183.07	151.39	6223.00	6879.53
	SD	225.81	253.42	279.22	113.36	7018.29	7720.27
Risperidone	Mean	73.07	86.60	88.78	146.81	8895.83	9384.56
per oral	SD	99.80	106.53	106.36	91.71	8204.93	8511.68
Other mono-Therapy	Mean	86.50	93.60	95.03	153.07	4941.18	5369.38
atypical	SD	82.39	85.14	85.68	144.58	3831.83	4081.86
Typicals	Mean	3.85	8.11	9.78	149.57	2887.50	3058.80
	SD	3.95	9.23	8.62	79.76	2250.83	2306.49
Combination	Mean	252.04	276.20	295.64	90.21	5288.89	6202.98
atypical-typical	SD	274.28	301.71	329.56	79.68	5499.14	6331.34

* included risperidone extended release (consta)
** typicals, other atypical monotherapy, combination typical-atypical

$3.85 for patients on typical antipsychotics. A similar pattern of differences in mean cost between patient groups was evident for antipsychotic medications. There were also interesting differences in the pattern of mean costs between the two teams. Patients treated by Team A had a considerably higher mean bed day cost than those treated by Team B while patients treated by Team B had a slightly higher mean cost for laboratory tests.

4.7.2 Relationship between the mean cost of antipsychotic agents and patients' characteristics

Because the cost data was not normally distributed, a natural logarithmic transformation was performed to normalize the cost measures.[93] The transformed data was analyzed with one-way analysis of variance with post-hoc comparison to determine whether age, length of stay, diagnosis and pattern of antipsychotic use influenced the antipsychotic, psychotropic, all drug and total costs. Meanwhile the

influence of gender and psychiatrist team toward these costs was analyzed with independent-samples t-test.

The independent-sample t-test of the mean cost of antipsychotic drugs found a statistically difference between female ($92.30±130.34) and male patients ($162.04± 208.62) (t=-3.267, p=0.001). The one-way analysis of variance of this mean cost showed statistically significant differences between patients in the different length of stay groups (F=46.710, p<0.001), by diagnosis (F=28.832; p<0.001) and pattern of antipsychotic use (F=3.181, p<0.015) (Table 4.18). These differences were further explored by conducting post-hoc comparisons using the Least Significant Difference (LSD) test.

Table 4.18 Analysis of the mean cost of antipsychotic medications

Independent variables	T	F	p-value
Gender	-3.267		0.001
Psychiatrist team	0.551		0.582
Age (years)		0.736	0.481
Length of stay (days)		46.710	0.000
Diagnosis		28.832	0.000
Antipsychotic use pattern		3.181	0.015

In terms of length of stay, the results indicated that the mean cost of antipsychotic medications for patients admitted for more than 10 days ($209.38±$216.38) was statistically significantly higher than for the two other LOS groups ($19.83±$15.08 and $58.76, ±$56.90) and that for patients admitted for 6 to 10 days was statistically significantly higher than for patients admitted for 5 or less days (Table 4.19).

Table 4.19 Post hoc test (Least Significant Difference) of the cost of antipsychotic medications cost based on patients' length of stay

(I) LOS	(J) LOS	Mean Difference (I-J)	p-value	95% Confidence Interval	
1-5	6-10	-0.832	0.004*	-1.390	-0.275
	>10	-2.163	0.000*	-2.632	-1.694
6-10	1-5	0.832	0.004*	0.275.	1.390
	>10	-1.331	0.000*	-1.792	-0.870
>10	1-5	2.163	0.000*	1.694	2.632
	6-10	1.331	0.000*	0.870	1.792
*Mean difference is significant at .05 ...					

In the case of type of antipsychotic medication, the mean cost of patients on combination atypical ($174.39±$213.26) was statistically significantly higher than on olanzapine ($93.10±98.89), quetiapine ($103.12±159.19) and risperidone (96.56±116.71) ($p<0.05$) but it was not difference with other groups ($152.50±225.81) (Table 4.20).

Table 4.20 Post hoc test (Least Significant Difference) of the cost of antipsychotic medications based on the pattern of antipsychotic use

(I) Antipsychotics	(J) Antipsychotics	Mean Difference (I-J)	p-value	95% Confidence Interval for Difference	
Others	Olanzapin only	0.784	0.059	-0.031	1.598
	Quetiapine only	0.226	0.467	-0.385	0.836
	Risperidon only	0.667	0.163	-0.272	1.605
	Combination atypical	-0.428	0.160	-1.028	0.171
olanzapin only	Others	-0.784	0.059	-1.598	0.031
	Quetiapine only	-0.558	0.173	-1.363	0.247
	Risperidon only	-0.117	0.830	-1.192	0.958
	Combination atypical	-1.212	0.003*	-2.009	-0.416
quetiapine only	Others	-0.226	0.467	-0.836	0.385
	Olanzapin only	0.558	0.173	-0.247	1.363
	Risperidon only	0.441	0.351	-0.489	1.371
	Combination atypical	-0.654	0.029*	-1.240	-0.067
risperidon only	Others	-0.667	0.163	-1.605	0.272
	Olanzapin only	0.117	0.830	-0.958	1.192
	Quetiapine only	-0.441	0.351	-1.371	0.489
	Combination atypical	-1.095	0.02*	-2.018	-0.172
combination atypical	Others	0.428	0.160	-0.171	1.028
	olanzapin only	1.212	0.003*	0.416	2.009
	Quetiapine only	0.654	0.029*	0.068	1.240
	Risperidon only	1.095	0.020*	0.172	2.018

*Mean difference is significant at .05 ...

Statistically significant differences were also found between diagnosis ($p<0.05$). Schizophrenia had the highest cost ($207.82±$217.44), followed by affective disorders ($129.64±$183.89) and other diagnoses ($44.72 ±$57.68) (Table 4.21).

Table 4.21 Post hoc test (Least Significant Difference) of the cost antipsychotic medications based on diagnosis

(I) diagnosis	(J) diagnosis	Mean Difference (I-J)	p-value	95% Confidence Interval	
schizophrenia	Affective disorder	0.896	0.000*	0.410	1.383
	Miscellaneous	1.810	0.000*	1.338	2.281
Affective disorder	Schizophrenia	-0.896	0.000*	-1.383	-0.410
	Miscellaneous	0.913	0.001*	0.398	1.429
miscellaneous	Schizophrenia	-1.810	0.000*	-2.281	-1.339
	Affective disorder	-0.913	0.001*	-1.429	-0.398

*Mean difference is significant at .05 ...

4.7.3 Relationship between the mean cost of psychotropic agents and patients' characteristics

The mean of cost of psychotropic drugs for treating female ($107.47±138.00) and male patients ($181.56±234.08) was statistically significantly different (t=-2.867, p=0.005). The one-way analysis of variance of the mean cost of psychotropic agents showed statistically significant differences in the mean cost for patients in the different length of stay groups (F=65.145, p<0.001), by diagnosis (F=27.664, p<0.001) and by antipsychotic use pattern (F=2.12, p=0.080) (Table 4.22).

Table 4.22 Analysis of the mean cost of psychotropic agents

Independent variables	T	F	p-value
Gender	-2.867		0.005
Psychiatrist team	0.641		0.522
Age (years)		0.939	0.393
Length of stay (days)		65.145	0.000
Diagnosis		27.664	0.000
Antipsychotic use pattern		2.121	0.080

Again these differences in mean cost were further explored. The result of the LSD test indicated that the mean cost of psychotropic agents between LOS groups were statistically significantly different (Table 4.23). The mean cost for patients with a

LOS of 6 to 10 days ($66.95±$59.21) was around three fold that of patients with a LOS of 1 to 5 days ($22.90±$16.91). Patients hospitalized for more than 10 days also had a mean cost that was statistically significantly higher ($236.72±$238.98) than the mean costs for patients in the other two LOS groups.

Table 4.23 Post hoc test (Least Significant Difference) of the cost of psychotropic agents based on patients' length of stay

(I) LOS	(J) LOS	Mean Difference (I-J)	p-value	95% Confidence Interval	
1-5	6-10	-0.901	0.000*	-1.369	-0.434
	>10	-2.164	0.000*	-2.557	-1.770
6-10	1-5	0.901	0.000*	0.433	1.369
	>10	-1.262	0.000*	-1.649	-0.876
>10	1-5	2.164	0.000*	1.770	2.557
	6-10	1.262	0.000*	0.876	1.649

*Mean difference is significant at .05 ...

In relation to differences in the cost of psychotropic agents for patients with different diagnoses, the mean cost for patients suffering schizophrenia was statistically significantly higher ($225.25±$235.75) than for patients with affective disorder ($159.02±$217.65) and other diagnoses ($52.73±$61.39) and was higher for patients with affective disorder than those with in the miscellaneous diagnosis category (Table 4.24).

Table 4.24 Post hoc test (Least Significant Difference) of the cost of psychotropic agents based on diagnosis

(I) diagnosis	(J) diagnosis	Mean Difference (I-J)	p-value	95% Confidence Interval	
schizophrenia	affective disorder	0.630	0.005*	0.193	1.067
	Miscellaneous	1.593	0.000*	1.170	2.016
affective disorder	Schizophrenia	-0.630	0.005*	-1.067	-0.193
	Miscellaneous	0.964	0.000*	0.501	1.426
miscellaneous	Schizophrenia	-1.593	0.000*	-2.016	-1.170
	affective disorder	-0.964	0.000*	-1.426	-0.501

*Mean difference is significant at .05 ...

4.7.4 Relationship between the mean cost of all drugs and patients' characteristics

In terms of the mean cost of all drugs, the mean cost of male patients ($191.99±251.40) was statistically significantly higher than female patients ($117.96±147.87). The one-way analysis of the cost of all drugs found statistically significant differences in mean costs for patients in the different length of stay groups and by diagnosis (Table 4.25).

Table 4.25 Analysis of the mean cost of all drugs

Independent variables	T	F	p-value
Gender	-2.558		0.011
Psychiatrist team	0.939		0.349
Age (years)		0.823	0.441
Length of stay (days)		64.765	0.000
Diagnosis		27.999	0.000
Antipsychotic use pattern		1.995	0.097

The results of the LSD tests indicated highly statistically significant differences ($p<0.001$) in mean costs based on the three groups of patient length of stay (Table 4.26). The mean cost of all drugs for patients who stayed in hospital more than 10 days ($251.79±257.32) was significantly higher than for the two other LOS categories ($26.41±21.40 and $72.51±60.70 for 1 to 5 days and 6 to 10 days respectively) and for patients who stayed in hospital between 6 and 10 days was statistically significantly higher those with a length of stay of 5 or less days.

Table 4.26 Post hoc test (Least Significant Difference) of the cost of all drugs based on patients' length of stay

(I) LOS	(J) LOS	Mean Difference (I-J)	p-value	95% Confidence Interval	
1-5	6-10	-0.948	0.000*	-1.404	-0.493
	>10	-2.122	0.000*	-2.506	-1.739
6-10	1-5	0.948	0.000*	0.493	1.404
	>10	-1.174	0.000*	-1.551	-0.797
>10	1-5	2.122	0.000*	1.739	2.506
	6-10	1.174	0.000*	0.797	1.551

*Mean difference is significant at .05 ...

The mean cost of all drug used by schizophrenic patients ($232.92±241.78) was statistically significantly higher than for other groups ($181.14±253.06 for affective disorders and $56.35±63.22 for other diagnoses) and for affective disorders was statistically significantly higher than for patients in the miscellaneous diagnosis category (Table 4.27).

Table 4.27 Post hoc test (Least Significant Difference) of the cost of all drugs based on diagnosis

(I) diagnosis	(J) diagnosis	Mean Difference (I-J)	p-value	95% Confidence Interval	
schizophrenia	affective disorder	0.562	0.010*	0.137	0.987
	miscellaneous	1.555	0.000*	1.144	1.966
Affective disorder	schizophrenia	-0.562	0.010*	-0.987	-0.137
	miscellaneous	0.993	0.000*	0.543	1.443
miscellaneous	schizophrenia	-1.555	0.000*	-1.966	-1.144
	affective disorder	-0.993	0.000*	-1.443	-0.543
*Mean difference is significant at .05 ...					

4.7.5 Relationship between the mean total costs and patients' characteristics

The one-way analysis of variance exploring differences in total costs showed that the significant differences in mean total cost were between patients in different age groups (F=3.500, p=0.032), in the different length of stay groups (F=284.353, P<0.001), and in different diagnosis group (F=25.356, p<0.001) (Table 4.28).

Table 4.28 Analysis of the mean of total treatment costs

Independent variables	T	F	p-value
Gender	-1.431		0.182
Psychiatrist team	1.946		0.053
Age (years)		3.500	0.032
Length of stay (days)		284.353	0.000
Diagnosis		25.356	0.000
Antipsychotic use pattern		0.523	0.719

The patients aged less than 35 years ($5,939.24±6,427.29) had a statistically lower mean total cost than patients in other age groups while patients in the 35-44 year group ($8,075.80±8,014.92) had a significantly higher mean total cost that those in the 35 years and less age group. The LSD test also indicated the mean total cost of the 35-44 year group was not significantly different from the mean total cost of patients aged more than 44 years ($7,238.94± 6,072.16) (Table 4.29).

Table 4.29 Post hoc test (Least Significant Difference) of the total cost based on age

(I) age	(J) age	Mean Difference (I-J)	p-value	95% Confidence Interval	
<35	35-44	-0.390	0.020*	-0.718	-0.061
	>44	-0.366	0.047*	-0.726	-0.006
35-44	<35	0.390	0.020*	0.061	0.718
	>44	0.024	0.903	-0.365	0.413
>44	<35	0.366	0.047*	0.006	0.726
	35-44	-0.024	0.903	-0.413	0.365
*Mean difference is significant at .05 ...					

The LSD tests showed highly statistically significant differences (p<0.001) in mean costs based on the three groups of patient length of stay (Table 4.30). The total mean cost of patients with a LOS of more than 10 days ($10,594.14±$7,288.83) was statistically significantly higher than for other groups ($3,119.81±$537.01 for the 6 to 10 days group and $1,196.47±$499.61 for 6 days group) meanwhile for patients who stayed in hospital between 6 and 10 days was statistically significantly higher those with a length of stay of 5 or less days.

Table 4.30 Post hoc test (Least Significant Difference) of the total cost based on patients' length of stay

(I) LOS	(J) LOS	Mean Difference (I-J)	p-value	95% Confidence Interval	
1-5	6-10	-1.040	0.000*	-1.253	-0.828
	>10	-2.101	0.000*	-2.280	-1.922
6-10	1-5	1.040	0.000*	0.828	1.253
	>10	-1.061	0.000*	-1.237	-0.885
>10	1-5	2.101	0.000*	1.922	2.280
	6-10	1.061	0.000*	0.885	1.237
*Mean difference is significant at .05 ...					

The LSD tests of total cost based on diagnosis indicated the mean total cost for schizophrenia patients ($9,169.50±7,301.52) was statistically significantly higher than for patients with affective disorder ($7,506.30±7,866.85) and patients in the miscellaneous group ($3,400.21±3,131.54), and for patients with affective disorders was statistically significantly higher than for patients in the miscellaneous diagnosis category. (Table 4.31).

Table 4.31 Post hoc test (Least Significant Difference) of the total cost based on diagnosis

(I) diagnosis	(J) diagnosis	Mean Difference (I-J)	p-value	95% Confidence Interval	
schizoprenia	Affective disorder	0.361	0.024*	0.049	0.673
	Miscellaneous	1.084	0.000*	0.782	1.386
Affective disorder	Schizophrenia	-0.361	0.024*	-0.673	-0.049
	Miscellaneous	0.723	0.000*	0.383	1.054
miscellaneous	Schizophrenia	-1.084	0.000*	-1.386	-0.782
	Affective disorder	-0.723	0.000*	-1.054	-0.393

*Mean difference is significant at .05 ...

5 Discussion

This study has examined the demographic and clinical characteristics of a cohort of psychiatric inpatients who were prescribed antipsychotic agents, their treatment patterns, and the cost of treatment.

Of psychiatric inpatients at this hospital, 70% were on antipsychotic medication. This finding was lower than reported in the studies by Paton et al [98], Bowers et al[57] and Mauri[1] (around 85%) but higher than the finding of the study by Botvinik et al (59%).[99] This use of antipsychotic medications was not surprising given the high proportion of patients with schizophrenia as the common indication of antipsychotic agents is treating psychotic symptom (amelioration of delusion and hallucination).[21, 38, 99]

5.1 Patient demographics

In this study the number of male patients (61%) was higher than the number of females (39%). This finding is consistent with the results of Botvinik's study[99] (64%) and slightly higher than Paton (59%)[98] and Bowers (58.2%)[57] studies. In contrast, Mauri et al[1] in their study conducted in 1999 and 2002 found the proportion of male patients was less than 50%.

The mean age of patients in current study (35.87±11.11 years) was younger than some previous studies,[1, 57] but consistent with the findings of a survey conducted by the Australian Bureau of Statistics in 2004-2005,[100] in which the prevalence of mental problems generally increased with age until the 35 t0 44 year age group and declined over this group.

Differences found in the age distribution of males and females could possibly be explained by differences in the onset and prevalence of disorders among females and males.[3, 33]

5.2 Clinical characteristics

The mean LOS in this study (18.0 ± 18.3 days) was shorter than that in the Bolvenik study (23.5 ± 21.9 days),[99] but similar to that reported in the Mauri study (16.36 ± 18.45 days).[1] The majority of patients in the current study were hospitalized for no more than 10 days. This relatively short LOS could be because most patients were treated with atypical drugs, as the first line treatment option for psychosis.[3]

In the current study, most patients were diagnosed with schizophrenia (40.7%), followed by affective disorder (bipolar disorder and depression), drug induced psychosis and personality disorder. A similar distribution of diagnoses among patients was found by Paton et al.[98]

The high proportion of patients with schizophrenia was not surprising because the common indication of antipsychotic agents is treating psychotic symptoms (amelioration of delusion and hallucination).[99] Because of its other indications, such as augmentation of antidepressants, relief of anxiety symptom and lessening of agitation (sedation), and control of behaviors (including self-harm and aggression) associated with personality disorders and mood stabilization, antipsychotic agents are also used in treating other disorders.[99]

5.3 Relationship between demographics and clinical characteristics

The relative number of women and men in each length of stay category was similar, which may reflect a similar level of severity of illness in both groups even though they had different patterns of diagnoses.

Although the length of stay of patients in different age groups was not statistically significantly different, older patients had a slightly longer hospital stay than younger patients. This could be because the onset of mental disorders is usually in the late teens through until around the 40s.[33] As a result, the severity of illness in older

patient is usually more severe than that in younger patients. In addition, younger patient are usually more tolerant to treatment with psychiatric drugs.

In this current study, the pattern of length of hospitalization of patient with each diagnosis was similar to the pattern found in the Davids study[45], in which patients with schizophrenia and affective disorder were treated longer than other patients. As one of the most disabling disorders,[3] it is not surprising that patients with schizophrenia had the longest time of length of hospitalization.

However, the duration of admission in this study was significantly shorter than those in Davids' previous study.[45] Patients with schizophrenia and affective disorders in the current study were treated for around 20 days but in Davids' study the patients stayed in hospital about 40 to 50 days. [45] In the case of patients with personality disorders and mental disorder due to psychoactive substance, in this study these patients were hospitalized for approximately eight days and ten days, respectively, while in Davids' the equivalent hospital episodes were around 29 and 13 days, respectively. The shorter length o stay in this study could be because the use of atypical drugs, which is associated with decreased psychiatric hospitalization rate, shortened length of stay per episode and fewer hospital days per year.[86] In current study 154 of 182 inpatients (84.6%) used atypical drugs while in the Davids patients fewer than 30% of the study patients used atypicals. In addition, data from the three reference years (1998, 2001 and 2003) in the Davids study showed increasing use of atypical antipsychotics for all diagnoses, which was concomitant with a decreasing length of stay.[45]

Severity of illness,[101, 102] treatment resistance,[103] diagnosis, [102, 104, 105] and gender[102, 104, 105] are factors that generally determine the duration of hospitalization. Schizophrenic patients or patients with affective disorders who are chronically ill and resistant to treatment usually need long treatment in hospital while drug induced psychosis wears off even without treatment after the illicit drugs had gone out of the patients' body. The atypical agents usually help to reduce psychosis and hence shorten the length of stay.

Psychiatrist team A and team B treated almost equal number of psychiatric patients in 2005. The length of stay of patients who were treated by each team were not statistically significantly different although the mean of stay of patients treated by team A was longer than that by team B (21.06 ± 21.20 days versus 14.08 ±. 12.93 days). This may be explained by team A treating more schizophrenia patients (48%) than team B (31.3%). Schizophrenia patients had the longest mean length of stay of all compared with patients with other diagnoses.[104]

In this study, the percentage of males and females who suffered each psychiatric disorder was statistically significantly different. While the incidence of schizophrenia and bipolar disorder is generally similar in both genders,[3, 21, 33] in this study, relatively fewer females were diagnosed with schizophrenia and bipolar disorders. The higher percentage of male inpatients suffering schizophrenia may be because of an earlier onset of this condition in men than women and women tend to have a better prognosis, a more benign course of illness, fewer hospital admissions and a better social functioning than men.[3, 21, 33]

In this study, drug induced psychosis was diagnosed relatively more in male than female patients, which is consistent with the incidence of this disorder with the difference found to be more marked for non-alcohol substance than alcohol. [33]

More patients in the personality disorder category suffered borderline personality disorder, followed with patient with antisocial disorder. Borderline personality disorder is twice as common in women as in men, while antisocial is more common in men than in women.[33]

Relatively more female patients were diagnosed with depression than males. This finding is similar with general population prevalence, with a twofold greater prevalence of depressive disorder in women than men.[33] The reasons for the difference have been hypothesized to involve hormonal differences, the effect of childbirth, differing psychosocial stressors for women and men, and behavioral models of learned helplessness.[33]

The patterns of patients' age across each diagnosis in this study were similar to a previous study.[45] Patients with affective disorder were the oldest and patients with drug induced psychosis were the youngest. One of reason for the latter is that the highest rate of abuse and dependence on substance is found among people in their late teen to early twenties with rates of use lower in older age groups.[33] Although these two studies had the same pattern of age by diagnosis, this study had a younger cohort of patients overall. In Davids study,[45] the mean age of patients with schizophrenia was around 43 years, affective disorder was 52 years, personality disorder was 35 years and 41 years was the mean age of people with neurotic, stress related and somatoform disorder. In this current study the age of patients with schizophrenia, effective disorders, drug induced psychosis and other diagnoses were 34, 41, 29 and 35 years old respectively.

5.4 Patterns of antipsychotic and other psychotropic medications

5.4.1 Medications as regular use

Psychotropic drugs regularly prescribed for psychoses in this study were similar with a previous study.[62] The most frequently prescribed were antipsychotics (mainly atypicals), followed by benzodiazepines, mood stabilizers, antidepressants and anticholinergics.

In this current study, the use of atypical antipsychotic medications (32.6%) was more than ten fold that of typical drugs (2.9%). Of 182 cases, 106 cases (58.2%) were treated with one atypical and only nine cases (4.9%) with one typical. Most patients were treated with a single atypical antipsychotic, which is the correct prescribing policy of this hospital. In addition, atypicals are as effective as the typicals in treatment of psychoses, but better tolerated because less likely to cause extrapyramidal side effects and also more efficacious for the negative symptoms and cognitive deficit.[3] Antipsychotics, which have a major effect on the reduction of psychotic symptoms, are effective for treating schizophrenia and also other psychiatric disorders namely bipolar disorder, depression with psychotic features, personality disorder, and substance-induced psychotic disorder.[1, 21, 33, 38, 57]

Combination atypical medications were also commonly prescribed for patients in this study, with 53 cases (29.1%) treated with these combinations. In contrast, only two cases (1.1%) were treated with combination typicals. Polytherapy by using typicals with atypical medication was quite often, accounting for 32 cases (17.6%). This finding differed from the finding in Paton's study,[71] which reported typical antipsychotics accounting for 51.6% of routine prescriptions. Other studies have shown that polypharmacy is common among patients with severe mental illness.[11, 83, 106] The results of these studies were similar to the current study in which antipsychotic polytherapy was common among males, patients less than 30 years old and schizophrenic patients.[11, 106] Although the majority of experts suggest monotherapy, polypharmacy is considered to be essential in specific cases such as treatment for high levels of agitation and danger to the patient himself or others, therapy resistance, non responsiveness to monotherapy, and avoidance of adverse events from high dosing of a single agent. [11, 46, 106]

Olanzapine was the most often prescribed as monotherapy and polytherapy with other antipsychotics. This finding is consistent with some previous studies[57, 98] but one other study reported that risperidone was used most commonly followed by haloperidol and olanzapine.[1] Both findings adhere with a consensus[3, 86, 1073, 86, 1073, 86, 107] that the newer antipsychotic medications, namely olanzapine, risperidone and quetiapine, should be the first-line treatment option for first episode and relapse of schizophrenia. [2, 59, 82] Quatiapine and risperidone were the second and third most often used in this current study, however the Paton's study reported clozapine and risperidone were the second and third, and quetiapine was the fifth atypical that most commonly used.[98]

The typical antipsychotic medication that was most commonly prescribed in this current study was chlorpromazine. This finding is similar with a previous study[98] that also found chlorpromazine was the most frequently used. Beside used as monotherapy, chlorpromazine also was frequently prescribed concurrently with other typical and atypical antipsychotics. Again this finding is similar with a previous study.[99] This use of chlorpromazine results from it being used as the

sedative agent of choice since it causes marked sedation and moderate extrapyramidal effects.[3]

Combination olanzapine with quetiapine and olanzapine with risperidone were the most common atypical polytherapy in this study. This finding was similar with the result of a study conducted by Centorrino et al.[67] However, in this latter study, a combination of olanzapine with haloperidol was the most frequently occurring combination,[67] while in the current study, olanzapine with chlorpromazine was the most frequently occurring.

Beside antipsychotics, other psychotropic medications, such as anxiolytic and hypnotic, antidepressants, mood stabilizers and anticholinergic medications were used for treating psychiatric patients. These drugs are used to diminish symptoms. Anxiolytics and hypnotic therapy treat anxiety, agitation and insomnia and its short-term use can be particularly useful in acute episodes.[3] Antidepressants are used when a depressive component of mental disorder is present.[3] Mood stabilizers are for treatment of mania.[3] Anticholinergics are commonly used to diminish extrapyramidal effects caused by the conventional antipsychotics. [3, 108]

5.4.2 Medications as PRN use

The pattern of drug use was slightly changed when medications on a PRN basis were included in the data. Although the use of medications as required prescription medication contribute to polypharmacy, high doses, side effects and dangerous drug interaction, this practice is common in inpatient psychiatric treatment.[11, 62, 63, 65, 109, 110]

Antipsychotics, anxiolytics and hypnotics, and anticholinergic drugs were psychotropics that were commonly prescribed as PRN drugs. The results of this study are similar to those reported in previous studies.[59, 62, 108] PRN antipsychotics, anxiolytics and hypnotics are usually used for managing acute psychosis in patient symptoms and behaviours while anticholinergics are for treating parkinsonian side effects. [62-64, 110]

While the research of Simon et al.[108] showed that non-psychotropics such as analgesics and drugs for gastrointestinal disorder were prescribed most commonly on a PRN basis, in this current research analgesics and salbutamol inhaler were most commonly prescribed. These medications treat the comorbidities.

5.4.3 Association between prescribing pattern of antipsychotics and patients' characteristics.

The only statistically significant difference in the pattern of use of antipsychotics was between diagnosis, with the difference largely explained by differences between the patterns of antipsychotics used for treating schizophrenic patients and the other two groups of patients (affective disorders group and miscellaneous group). Patients with schizophrenia were treated relatively more frequently with risperidone, combination atypicals and other monotherapy atypicals than patients with affective disorder and miscellaneous disorders. On the other hand, patients with affective disorder and other disorders were treated relatively more frequently with olanzapine and quetiapine.

Further investigation indicated that the odd of schizophrenic patients being treated with risperidone rather than olanzapine was 4.348 times higher than for patients with other diagnoses (drug induced psychosis, personality disorder, miscellaneous group). The odds of schizophrenic patients being treated with combination atypicals rather than olanzapine was also 5.388 times higher than patient in other diagnoses.

When PRN antipsychotic drug were included in the data, the patterns of treatment differed between diagnoses and also between psychiatrist teams. Combination atypicals were most frequently for patients diagnosed with schizophrenia while two other groups of diagnoses were most commonly prescribed olanzapine. Schizophrenic patients were 6.178 times more likely to be on combination atypicals rather than olanzapine when compared with patients with miscellaneous diagnoses. When the psychiatrist team B was compared with the team A, team B preferred to use olanzapine to miscellaneous antipsychotics (other monotherapy atypical, typical, combination atypical-typical) (odds=2.915).

Although clinicians usually use atypical antipsychotics such as risperidone and olanzapine as first-line treatment for psychotic episode,[3, 111] the results discussed above cannot conclude that the effectiveness of risperidone or combination atypicals is superior to olanzapine since the comparative effectiveness amongst atypicals is debatable. [3, 111] In addition, diagnosing psychiatric disorders diagnoses is complicated and sufficient information not always provided to determine appropriate drugs.[69] For determining treatment for each patient, physicians should base their decisions on the clinical characteristics of the patient and drug properties.[3]

5.5 Economic analysis

The economic analysis of treatment costs showed that the mean of costs for treating male patients were higher than females, and these differences were statistically significant for the cost for antipsychotics, psychotropics, and all drugs. This may have resulted from the longer length of stay of male patients and the higher number of male patients suffering schizophrenia.

Although the costs for antipsychotics, psychotropics, all drugs and total expenditure between psychiatrist team A and B were not statistically significant, the patients were treated by team A had higher costs than team B. This finding may also be a result of the relative higher number of schizophrenic patients treated by team A.

The patients aged more than 44 years had the lowest mean costs of antipsychotics, psychotropics, and all drugs while the patients aged less than 35 years had the lowest mean total cost. The age group with the highest costs in all cost categories was the 33 to 44 year old group in which almost half the patients suffered from schizophrenia and this group also had the highest length of stay.

In terms of length of stay, the results indicated that the mean costs of patients admitted for one to five days were a tenth of the costs of patients who were hospitalized more than ten days and around a third of the costs of patients who were hospitalized 5 to 10 days.

The costs for treatment schizophrenic patients were the highest, followed by affective disorders and other diagnoses. A study in USA also found that psychosis diagnosis was associated with higher treatment costs. [86]

The above results show that length of stay and a schizophrenia diagnosis influence the costs. Longer stays in hospital automatically lead to increase in other costs such as drugs and laboratory tests.[79] Since hospitalization is the greatest contributor to the direct costs,[10, 79, 80] a reduction in hospital use would have an important impact on the overall costs of the illness.[81]

Compared with other psychiatric disorders, schizophrenic patients usually use more inpatient facilities.[75, 86] The study by Garattini et al also found that the cost associated with drug therapy and laboratory tests for patients with related psychotic disorder were significantly higher than these costs for other patients.[75]

The mean cost of antipsychotic medications for treating patients on olanzapine, quetiapine, risperidone, combination atypical and other antipsychotics (other atypical mono therapy, typicals, combination atypical-typical antipsychotics) were different significantly. While the mean costs of antipsychotics, psychotropics, and all drugs for patients on combination atypical were the highest, risperidone had the highest of the total cost because of patients on this drug were hospitalized longer than others. A previous study show different figures. [86] In this study, the highest total cost was for olanzapine users because this group had the highest inpatient use while the users of combination of atypicals had the lowest total cost.[86] Although the cost of antipsychotic medications comprise a minor portion of the direct costs of schizophrenia, they can have the major impact on costly aspects of care such as hospital admission.[10]

5.6 Study limitations and area of future research

The limitations and recommendations for future research of this study were as follows-

- It was a retrospective study using existing data that have been recorded for reasons other than research. The accuracy of the data therefore relied on accuracy of the written record.
- This study examined a relatively small sample size and reflected the trends in a single psychiatric ward in Western Australia in 2005. For this reason, the findings may not be generalizable to treatment of all psychiatric inpatients who are prescribed antipsychotic agents.
- Prescribing post discharge was not evaluated so that the findings cannot be extrapolated to treatment setting outside of the hospital.
- This study did not collect data on characteristics of prescribing physicians, patient symptoms, symptom severity, outcome measures, secondary diagnoses, adverse effects, medication post discharge, total daily doses and whether the patients were first or subsequent admissions to the unit. Future studies examining the use of antipsychotics in hospital inpatient settings should include these items in their data collection in order to allow a more detailed evaluation of differences in the pattern of antipsychotic use and corresponding costs.
- This study did not address questions relating to the appropriateness of prescribing practices by making a comparison with recommended or standard therapy for use of psychotropic medications in National Therapeutic Guidelines for psychotropic prescribing (e.g. eTGs). Assessing appropriateness of therapy is important but the question of appropriateness was outside the scope of the study. In order to assess appropriateness, additional data would have been required including patient symptoms, severity of symptoms, secondary diagnoses, outcome measures and the like. It is recommended that future studies be conducted to address the question of the appropriateness of prescribing practices of antipsychotics for hospital inpatients.

In this study, chi-squared analysis and multinomial logistic regression used to determine the differences between demographic and clinical features, and the patterns of clinical use of antipsychotic medications. This analysis identify the differences but they do not provide the ability to determine specifically where the difference is per se. Using more sophisticated statistical analysis are recommended for future research in this area where there are multiple variables.

6 Conclusion

Through reviewing the medical records of psychiatric patients who were admitted to AKMH in 2005, this study found the number of male patients was higher than the number of females and their mean age of all patients was 35.87±11.11 years. More than half of the patients were admitted to hospital for more than 10 days with the mean length of stay of 18.0 ± 18.3 days. Patients treated by psychiatrist team A were hospitalized longer than those by team B and team A treated more schizophrenic patients than team B. The most common diagnosis was schizophrenia. This finding is not surprising as the main indication of antipsychotics is for treating psychosis.

In this study the use of atypical antipsychotics as the first line treatment of psychosis was more than tenfold that of typical drugs. These findings confirmed the trend of the use of atypical and typical antipsychotic medications, in which there is an increasing trend of atypical use and decreasing trend of typical use. In addition to antipsychotic medications; anxiolytic, hypnotic and anticholinergic drugs were given as needed drugs. This is a common practice in hospital although this practice contributes to polypharmacy, high doses, side effects and dangerous drug interactions.

Only diagnosis influenced the prescribing patters of antipsychotics. Patients with schizophrenia were treated relatively more commonly with risperidone and combination atypicals than patients with affective disorder and miscellaneous disorders. Meanwhile these latter disorders were treated relatively more frequently with olanzepine and quetiapine.

With regards to costs, schizophrenic patients had the highest mean cost per patient, largely because of their longer length of stays. Patients with schizophrenia also had the highest mean cost for drugs, including both antipsychotics and psychotropic drugs.

The findings of this thesis in relation to the prescribing patterns of antipsychotic and other medications to psychiatric patients, the corresponding costs, and factors influencing prescribing patterns enables a better understanding to be gained of the

profile of admitted psychiatric patients and their treatment. In a hospital environment with limited budgets, this information is useful for both psychiatrists and pharmacists in the future management of patients and in decisions relating to the allocation of the pharmacy budget.

References

1. Mauri MC, Regispani F, Beraldo S, Volonteri LS, Ferrari VM, Invernizzi G. Patterns of clinical use of antipsychotics in hospitalized psychiatric patients. Prog Neuropsychopharmacol Biol Psychiatry 2005;29:957-63
2. Simpson GM. Atypical antipsychotics and the burden of disease. Am J Manag Care. 2005;11(8):S235-41.
3. Anonim. Therapeutic Guidelines: Psychotropic. Victoria: Therapeutic Guidelines Limited 2003. p. 1-37, 99-153.
4. Castle D, Alderton D. Psychopharmacological management of schizophrenia In: Castle D, Copolov DL, Wykes T, editors. Pharmacological and Psychological Treatments in Schizoprenia. London: Martin Dubitz; 2003. p. 1-22.
5. Oliveira IR, Juruena MF. Treatment of psychosis: 30 years of progress. J Clin Pharm Ther. 2006;31:523-34.
6. Rosenheck R. The growth of psychopharmacology in the 1990s: evidence-based practice or irrational exuberance. . Int J Law Psychiatry 2005;28:467-83.
7. Patel NC, Crismon ML, Hoagwood K, Johnsrud MT, Rascati KL, Wilson JP. , et al. Trends in use of typical and atypical antipsychotics in children and adolescents. J Am Acad Chil Adolesc Psychiatri 2005;44(6):548-56.
8. Mond J, Morice R, Owen C, Karten A. Use of antipsychotic medication in Australia between july 1995 and December 2001. Aust N Z J Psychiatry. 2003(37):55-61.
9. Hollingworth S, Siskind D, Nissen L, Robinson M, Hall W. Patterns of antipsychotic medication use in Australia 2002-2007. Aust N Z J Psychiatry. 2010(44):372-7.
10. Hudson TJ, Sullivan G, Feng W, Owen RR, Thrush CR. Economic evaluations of novel antipsychotic medications: a literature review. Schizophr Res. 2003;60:199-218.
11. Lelliott P, Paton C, Harrington M, Konsolaki M, Sensky T, Okacha C. The influence of patient variables on polypharmacy and combined high dose of antipsychotic drugs prescribed for in-patients. Psychiatr Bull. 2002;26:411-4.
12. Harington M, Lelliott P, Paton C, Okocha C, Duffett R, Sensky T. The results of a multi-centre audit of the prescribing of antispychotic drugs for in-patients in the UK. Psychiatr Bull. 2002;26:414-8.
13. Moore TA, Covell NH, Essock SM, Miller AL. Real-world antipsychotic treatment practices. Psychiatr Clin N Am. 2007;30:401-16.
14. Castle D, Morgan V, Jablensky A. Antipsychotic use in Australia: the patients' perspective. Aust N Z J Psychiatry 2002;36:633-41.
15. Lane HY, Chang YC, Chiu CC, Chen TT, Lee SH, Chang WH. Influences of patient-related variaables on risperidone efficacy for acutely exacerbated schizoprenia: analyses with rigorous statistics. J Clin Psychopharmacol 2002;22:353-.
16. Lieberman JA, Koreen AR, Chakos M. Factors influencing treatment response and outcome of first episode schizoprenia: implications for understanding the pathophysiology of schizoprenia. J Clin Psychiatry 1996;57(suppl 9):5-9.
17. Reeves S, Stewart R, Howard R. Service contact and psychopathology in very-late-onset schizoprenia-like psychosis: the effects of gender and ethicity. Int J Geriatr Psychiatry 2002;17:473-9.

18. Ziguras S, Lambert TJR, McKenzie DP, Pennella J. The influence of client's ethnicity on psychotropic medication management in community mental health services. Aust N Z J Psychiatry 1999;33:882-8.
19. Gardner DM, Baldessarini RJ, Waraich P. Modern antipsychotic drugs:a critical overview. CMAJ. 2005;172(13):1703--11.
20. Knapp MRJ. Measuring the economic benefit of treatment with atypical antipsychotics. Eur Psychiatry. 1998;13(Suppl 1):37s-45s.
21. Mueser KT, McGurk SR. Schizoprenia. Lancet. 2004;363:2063-72. .
22. dosReis S, Johnson E, Steinwachs D, Rohde C, Skinner EA, Fabey M, et al. Antispychotic treatment patterns and hospitalizations among adults with schizoprenia. Schizophr Res. 2008;101:304-11.
23. Fleischhacker WW. Second-generation antipsychotics: are their similarities greater than their differences? . Eur Psychiatry 2003;18:38s-45s.
24. Palmer CS, Brunner E, Ruiz-Flores LG, Paez-Agraz F, Revicki DA. A cost-effectiveness clinical decision analysis model for treatment of schizoprenia. Arch Med Res 2002;33:527-80.
25. Drew LRH, Hodgson DM, Griffiths KM. Clozapine in community practice: a 3-year follow-up study in the Australian Capital Territory. Aust N Z J Psychiatry 1999;33:667-75.
26. Anderson DM, Keith J, Novak PD, Elliot MA. Mosby's Medical, nursing, and allied health dictionary. 6th ed. Missouri: Mosby, Inc.; 2002. p. 1080, 119, 426.
27. Anonim. Diagnostic and statistical manual of mental disorders: DSM-IV-TR. . 4th ed. Washington, DC: American Psychiatric Association; 2003. p. 41-8.
28. Galvin PM, Knezek LD, Rush AJ, Toprac MG, Johnson B. Clinical and economic impact of newer versus older antipsychotic medications in a community mental health center. Clin Ther 1999;21(6):1105-16.
29. Gelder M, Dennis G, Mayou R. Concise Oxford textbook of Psychiatry. Oxford: Oxford University Press 1994. p. 163-83, 95-213.
30. Frangou S, Kington J. Schizophrenia. Medicine 2004;32(7):21-5.
31. Anonim. The International Statistical Classification of Disease and related health problems, Australian Modification (ICD-10-AM). 10th ed. Sydney: National Centre for Classification in Health; 1998. p. 89-131.
32. First MB, Tasman A. DSM-IV-TR mental disorders: diagnosis, etiology, and treatment. West Sussex: John Wiley & Sons, Ltd. ; 2004. p. 8-52, 354-693, 736-69, 97-811, 1230-6.
33. Kaplan HI, Benjamin JS. Kaplan and Sadock's Synopsis of Psychiatry: Behavioral Sciences/Clinical psychiatry. 8th ed. Maryland: Williams and Wilkins; 1998. p. 375-495, 524-80, 775-96
34. Keltner NL, Feldman JM. Drugs for schizoprenia and other psychoses. In: Keltner NL, Folks DG, editors. Psychotropic drugs. 4th ed. Missouri: Elsevier Mosby; 2005. p. 98-138, 92-227.
35. Tyrer P. Personality disorders. Medicine 2004;32(7):26-8.
36. Macmillan I, Young AH, Ferrier IN. Mood (affective) disorders. Medicine 2004;32(7):14-6.
37. Leigh D, Pare CMB, Marks J. A concise encyclopaedia of psychiatry. Lancaster: MTP Press, Ltd; 1977. p. 90-1
38. Rosenbaum JF, Arana GW, Hyman SE, Labbata LA, Fava M. Handbook of psychotropic drug therapy. Philadelphia: Lippincott & Wilkins; 2005. p. 5-168, 75-201, 80-92.

39. Keltner NL, Folks DG. Psychotropic drugs. 4th ed. Missouri: Elsevier Mosby; 2005. p. 192-227.
40. Fountoulakis KN, Vieta E, Sanchez-Moreno J, Kaprinis SG, Goikolea JM, Kaprinis GS. Treatment guidelines for bipolar disorder: a critical review. J Affect Disord. 2005;86:1-10.
41. Post RM. Differing psychotropic profiles of the anticonvulsants in bipolar and other psychiatric disorders. Clin Neurosci Res. 2004;4:9-30.
42. Poole R, Brabbins C. Drug induced psychosis. Br J Psychiatry. 1996;168:135-8.
43. Fogarty A, Lingford-Hughes A. Addiction and substance misuse. Medicine. 2004;32(7):29-34.
44. Gregg L, Barrowclough C, Haddock G. Reason for increased substance use in psychosis. Clin Psychol Rev. 2007;27:494-510.
45. Davids E, Bunk C, Specka M, Gastpar M. Psychotropic drug prescription in a psychiatric university hospital in Germany Prog Neuropsychopharmacol Biol Psychiatry. 2006;30:1109-16. .
46. Rittmannsberger H, Meise U, Schauflinger K, Horvath F, Donat H, Hinderhuber H. Polypharmacy in psychiatric treatment, Patterns of psychotropic drug use in Austrian psychiatric clinics. Eur Psychiatry. 1999;17:1-8.
47. Anonim. Australian Medicines Handbook 2005. Adelaide: Australian Medicines Handbook 2005. p. 685-724.
48. Tyrer P. What's new in psychiatry: personality disorders. Medicine. 2005;33(7):1-3.
49. Reynolds GP. What's new in the neurochemistry of schizoprenia. Medicine. 2006;34(4):1-4.
50. Stahl SM. Selecting an atypical antipsychotic by combining clinical experience with guidelines from clinical trials. J Clin Psychiatry 1999;60(Suppl 10):31-41.
51. Thomas C, Lewis. S. Which atypical antipsychotic? . Br J Psychiatry 1998;172:106-9
52. Lieberman JA, Mendelowitz AJ. Antipsychotic drugs. In: Lieberman JA, Tasman A, editors. Psychiatric drugs. 1st ed. Pennsylvania: W.B. Saunders Company; 2000. p. 41-2.
53. Nash J, Potokar J. Anxiety disorders. Medicine. 2004;32(7):17-21.
54. Jordanova J, Maric NP, Alikaj V, Bajs M, Cavic T, Iosub D, et al. Prescribing practices in psychiatric hositalls in Eastern Europe. Eur Psychiatry. 2011;26:414-8.
55. Volkow ND, Li T-K. Drugs and alcohol: treating and preventing abuse, additiction and their medical sonsequences. Pharmacol Therapeut. 2005;108:3-17.
56. Swift RA, Peers EA, Jones BL, Bronson MV. Utilisation of a purposes-designed chart for the nursing management of acute alcohol withdrawal in the hospital seetting. Australas Emergen Nurs J. 2010;13:70-7.
57. Bowers L, Callaghan P, Clack N, Evers C. Comparisons of psychotropic drug prescribing patterns in acute psychiatric across Europe. Eur J Clin Pharmacol 2004;60:29-35.
58. Rittmannsberger H. The use of drug monotherapy in psychiatric inpatient treatment. Prog Neuropsychopharmacol Biol Psychiatry. 2002;26:547-51.
59. Keith J. Advances in psychotropic formulations. Prog Neuropsychopharmacol Biol Psychiatry. 2006;30:996-1008.

60. Shajahan P, Crighton J, Bashir M, Taylor M. Who respond to risperidone and zuclopenthixol long-acting injections? A compartive observational study. . Eur Psychiatry. 2007;22:S167.
61. Rubio G, Martinez I, Ponce G, Jimenez-Arriero MA, Lopez-Munoz F, Alamo C. Long-acting injectable risperidone compared with zuclopenthixol in the treatment of schizoprenia with substance abuse comorbidity. Can J Psychiatry 2006;51(8):531-8.
62. Geffen J, Sorensen L, Stokes J, Cameron A, Rebert MS, Geffen L. Pro re nata medication for psychosis: an audit of practice intwo metropolitan hospitals. Aust N Z J Psychiatry. 2002;36:649-56.
63. Geffen J, Cameron A, Sorensen L, Stokes J, Roberts MS, Geffen L. Pro re nata medication for psychoses: the knowledge and beliefs of doctors and nurses. Aust N Z J Psychiatry. 2002;36:642-8.
64. Dean AJ, McDermott BM, Marshall RT. PRN sedation-patterns of prescribing and administration on a child and adolescent mental health inpatient service. Eur Child Adolesc Psychiatry. 2006;15(5):277-81.
65. Parepally H, Chakravorty S, J L, Brar JS. The use of concomitant medications in psychiatric inpatients treated with either olanzepine or other antipsychotic agents: A naturalistic study at a state psychiatric hospital. Prog Neuropsychopharmacol Biol Psychiatry. 2002;26:437-40.
66. Centorrino F, Eakin M, Bahk WM, Kelleher JP, Goren J, Salvatore P. et al. Inpatient antipsychotic drugs use in 1998, 1993, and 1989. Am J Psychiatry 2002;159:1932-5.
67. Centorrino F, Goren JL, Hennen J, Salvatore P, Kelleher JP, Baldessarini RJ. Multiple versus single antipsychotic agents for hospitalized patients: case-control study of risks versus benefits. Am J Psychiatry 2004;161:700-6. .
68. Domino ME, Frank RG, Rosenheck R. The diffusion of new antipsychotic medications and formulary policy. Schizophr Res 2003;29(1):95-104.
69. Hadsall RS, Freeman RA, Norwood GJ. Factor related to the prescribing of selected psychotropic drugs by primary care physicians. Soc Sci Med. 1982;16:1747-56.
70. Hemminki E. Review of literature on the factors affecting drug prescribing. Soc Sci Med 1975;9:111-5.
71. Knapp M, Mangalore R, Simon J. The global costs of schizophrenia. Schizophr Res 2004;30(2):279-93.
72. Elliot R, Payne K. Essentials of economic evaluation in healthcare. London: The Pharmaceutical Press 2005. p. 45-63.
73. Walley T, Haycox A, Boland A, editors. Pharmacoeconomics. 1st ed. Edinburgh: Churchill Livingstone 2004.
74. Hirschfeld RMA, Vornik LA. Bipolar disorder-costs and comorbidity. Am J Manag Care 2005;11(3 Sup):S85-S90.
75. Garattini L, Barbui C, Clemente L, Cornago D, Parazzini F. Direct costs of schizoprenia and related disorders in Italian community mental health services: a multicenter, prospective 1-year follow up study. Schizophr Res. 2004;30(2):295-302.
76. Mallarkey G. Opinion and evidence: Pharmacoeconomics. Hong Kong: Adis International Limited 1999. p. 163-78.
77. Wulkan PD. New generation psychiatric medications Nevada: Devision of Mental Health and Development Services. [6 July 2007
]; Available from: http://mhfd.state.nv.us/pdfs/NGM02150.pdf.

78. WHO. Results of Unit Costs for patient services for the 14 GBD Regions: World Health Organization 2007 6 July 2007 Available from: http://www.who.int/choice/costs/unit_regions/en/.
79. Butler JRG. Hospital cost analysis. Dordrecht: Kluwer Academic Publishers; 1995. p. 1-5.
80. Knapp M, Kavanagh S. Economic outcome and costs in the treatment of schizoprenia. Clin Ther. 1997;19(1):128-38.
81. Mojtabai R, Lavelle J, Gibson JP, Bromet EJ. Atypical antipsychotics in first admission schizoprenia: medication continuation and outcomes. Schizophr Res 2003;29 (3):519-30.
82. Taylor D. Schizophrenia. In: Taylor D, Knapp M, Kerwin R, editors. Pharmacoeconomics in psychiatry. London: Martin Dunitz 2002. p. 19-42.
83. Percudani M, Barbui C. Cost and outcome implications of using typical and atypical antipsychotics in ordinary practice in Italy. J Clin Psychiatry 2003;64:1293-9.
84. Stensland MD, Jacobson JG, Nyhuis A. Service utilization and associated direct costs for bipolar disorder in 2004: An analysis in managed care. J Affect Disord 2007;101:187-93.
85. Kerwin R. Evidence and practice. In: Taylor D, M Ma, Kerwin R, editors. Pharmacoeconomics in psychiatry. London: Martin Dunitz 2002. p. 89-99.
86. Rothbard A, Murrin MR, Jordan N, Kuno E, McFarland BH, Stroup TS. , et al. Effects of antispychotic medication on psychiatric service utilization and cost. J Ment Health Policy Econ 2005;8:83-93.
87. Johnsrud MT, Crismon ML, Thompson A, Grogg. AM. An economic comparison of risperidone and olanzepine use within an integrated managed mental health program. Adm Policy Ment Health Ment Health Ser Res 2005.
88. Rabinowitz J, Lichtenberg P, Kaplan Z. Comparison of cost, dosage and clinical preference for risperidone and olanzepine. Schizophr Res. 2000;46:91-6.
89. Percudani M, Barbui C, Beecham J, Knapp M. Routine outcome monitoring in clinical practice: service and non-service costs of psychiatric patients attending a Community Mental Health Centre in Italy. Eur Psychiatry 2004;19:469-77.
90. Percudani M, Fattore G, Belloni GC, Gerzeli S, Contini A. Service utilisation and costs of first-contact patients in a community psychiatric service in Italy. Eur Psychiatry 2002;17:434-42.
91. Anonim. Western Australia Goverment Drug Tender, Contract No 5504: Supply of drugs, disinfectants & antiseptics and nutrition products.2005.
92. Anonim. Pathology Service: Department of Health and Ageing; 2004 2004 [cited 3rd November]. Available from: http:/www.health.gov.au/internet/wcms/publishing.nsf/content/DF8F565ADA574FDCA2571CCOO0AC149/$FIK/MB5%20Book%20I%202004%20Category%206.pdf.
93. Coakes SJ. SPSS version 12.0 for Windows: Analysis without anguish. Milton, Qld John Wiley & Sons Australia 2005. p. 28-43.
94. Field A. Discovering statistic using SPSS. 2nd ed. London: SAGE Publication 2005. p. 527-9, 681-94.
95. Glick HA, Joshi DA, Sonnad SS, Polsky D. Economic evaluation in clinical trials. Handbooks in health economic evaluation. Oxford Oxford University Press; 2007.
96. Australian Bureau of Statistics. National Regional Profile: Armadale (C) (Statistical Local Area). Population and people characteristics. Canberra. 2006.

97. Burns N, Grove SK. The practice of nursing research. 4th ed. Philadelphia: Saunders; 2001. p. 569-74.
98. Paton C, Lelliott P, Harrington M, Okacha C, Sensky T, Duffett R. Patterns of antipsychotic and anticholinergic prescribing for hospital inpatients. J Psychopharmacol. 2003;17(2):223-9.
99. Botvinik L, Ng C, Schweitzer I. Audit of antipsychotic prescribing in a private psychiatric hospital. Australasian Psychiatry 2004;12(3):227-33. .
100. Australian Bureau of Statistics. Mental health in Australia: a snapshot, 2004-05. 2006. Canberra: cat. no 4824.
101. Furlanetto LM, Silva TVd, Bueno JR. The impact of psychiatric comorbidity on length of stay of medical inpatients. Gen Hosp Psychiatry 2003;25:14-9.
102. Rothbard AB, Schinnar AP. Community determinants of psychiatric hospitalization and length of stay. Socio-Econ Pharm Sci. 1996;30(1):27-38.
103. Conley RR, Buchanan RW. Evaluation of treatment-resistant schizoprenia. Schizophr Res. 1997;23(4):663-74.
104. Chung W, Cho WH, Yoon CW. The influence of institutional characteristics on length of stay for psychiatric patients: a national database study in South Korea. Soc Sci Med. 2009;68:1137-44.
105. Chung W, Oh SM, Suh T, Lee YM, Oh BH, Yoon CW. Determinants of length of stay for psychiatric inpatients: analysis of a national database covering the entire Korean elderly population. Health Policy. 2010;94:120-8.
106. Morrato EH, Dodd S, Oderda G, Haxby DG, Allen R, Valuck RJ. Prevalence, utilization patterns, and predictors of antispychotic polypharmacy: experience in a Multistate Medicaid population, 1998-2003. Clin Ther. 2007;29(1):183-95.
107. Mladsi DM, Grogg AL, Irish WD, Lopez RB, Degan K, Swann A, et al. Pharmacy cost evaluation of risperidone, olanzepine,and quetiapine for the treatment of schizoprenia in acute care inpatient settings. Curr Med Res and Opin. 2004;20(12):1883-93.
108. Davies SJC, Lennard MS, Ghahramani P, Pratt P, Robertson A, Potokar J. PRN prescribing in psychiatric inpatient-potential for pharmacokinetic drug interactions. J Psychopharmacol. 2007;21(2):153-60.
109. Baker JA, Lovell K, Harris N. The impact of a good practice manual on professional practice associated with psychotropic PRN in acute mental health wards: An exploratory study. Int J Nurs Study. 2008;45:1403-10.
110. Hilton MF, Whiteford HA. Pro re nata medication for psychiatric inpatients: time to act. Aust N Z J Psychiatry. 2008;42:555-64.
111. Heres S, Davis J, Maino K, Jetzinger E, Kissling W, Leucht S. Why olanzepine beats risperidone, risperidone beat quetipine, and quetiapine beats olansepine: an exploratory analysis of head-to-head comparison studies of second-generation antispychotics. Am J Psychiatry. 2006;163:185-94.

Appendices

Appendix 1 Human Research Ethics Committee approval from Curtin University of Technology

Curtin
University of Technology

minute

To	Arie Sulistyarini
From	Mrs Jennifer Ramsay Ethics Committee Secretary
Subject	Protocol Approval **PH-09-2006**
Date	20 June 2006
Copy	Professor Michael Garlepp Ms Delia Hendrie Mr Steven Lim

Division of Heath Sciences

School of Pharmacy
GPO Box U1987
Perth WA 6845
Telephone +61 8 9266 7528
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Thank you for your "Form C Application for Approval of Research with Minimal Risk (Ethical Requirements)" for the project titled "**THE PATTERNS OF USE AND ECONOMIC ANALYSIS OF ANTIPSYCHOTIC MEDICATIONS IN TREATING HOSPITALIZED PSYCHIATRIC PATIENTS**". On behalf of the Human Research Ethics Committee I am authorised to inform you that the project is approved.

Approval of this project is for a period of eight months from **20 June 2006** to **28 February 2007**.

If at any time during the eight months changes/amendments occur, or if a serious or unexpected adverse event occurs, please advise me immediately. The approval number for your project is **PH-09-2006**. *Please quote this number in any future correspondence.*

Mrs Jennifer H. Ramsay
Committee Secretary
Human Research Ethics Committee

Please Note: The following standard statement must be included in the information sheet to participants:
This study has been approved by the Curtin University Human Research Ethics Committee. If needed, verification of approval can be obtained either by writing to the Curtin University Human Research Ethics Committee, c/ - Office of Research and Development, Curtin University of Technology, GPO Box U1987, Perth, 6845 or by telephoning 9266 2784.

Appendix 2 Human Research Ethics Committee approval from South Metropolitan Area Health Services

Department of Health

South Metropolitan Area Health Service

HUMAN RESEARCH ETHICS COMMITTEE

sd
06/236

30 June 2006

Mr S Lim
Chief Pharmacist
Armadale Health Service

Dear Stephen

Re: The Patterns of Use and Economic Analysis of Antipsychotic Medications in Treating Hospitalised Psychiatric Patients.

Further to my correspondence dated 21 June 2006, I am writing to confirm that on 26 June 2006 the Chief Executive, under delegated authority from the Minister for Health incorporated as the Board of the hospitals formerly comprised in the Metropolitan Health Service Board, endorsed the South Metropolitan Area Health Service (SMAHS) Human Research Ethics Committee's (HREC) recommendation to approve the above study.

As you know, the HREC is bound by NHMRC Guidelines to monitor the progress of all approved projects until completion, to ensure they continue to conform to approved ethical standards. You will, therefore, be required to submit an annual report on the progress of the study and a final report on completion. You are also required to advise the Committee of all events that occur and may affect the conduct of the study.

Would you please note that, should it be necessary at any stage of the study for an amendment to be made to the protocol, when submitting the amendment to the Committee you should provide, in a covering letter, a statement outlining to the Committee the significance of the change/s.

An annual report on this study is due in June 2007.

Please quote the following reference number on any future correspondence with the Committee regarding this protocol: **06/236**.

Yours sincerely

DR NORMA NICKEL
CHAIR
HUMAN RESEARCH ETHICS COMMITTEE

South Metropolitan Area Health Service
c/- Fremantle Hospital and Health Service
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Appendix 3 Research Publication

This study was presented as poster presentations at:

1. Annual Conference of the Australasian Pharmaceutical Science Association (APSA) in Adelaide, Australia, 3-5 December 2006

THE PATTERNS OF USE OF ANTIPSYCHOTIC MEDICATIONS IN TREATING HOSPITALIZED PSYCHIATRIC PATIENTS

Arie Sulistyarini[1], Delia Hendrie[2], Michael Garlepp[1], Stephen Lim[3], Alexander John[3]

[1]School of Pharmacy, Curtin University of Technology; [2]School of Population Health, University of Western Australia; [3]Armadale Kelmscott Memorial Hospital, Western Australia

Background: Prescribing patterns of antipsychotic medications have changed over time. Underlying the increasing use of antipsychotics is the dramatic increase in the prescribing of atypical antipsychotics, with the use of typicals decreasing. **Aim:** The aim of this study was to evaluate the use of antipsychotics in treating hospitalized psychiatric patients at the Adult Psychiatry In-patient Unit, Armadale Kelmscott Memorial Hospital in 2005. **Method:** The medical records of hospitalized psychiatric patients who were treated with antipsychotic medications in 2005 were reviewed retrospectively. Data relating to patients' age, gender, diagnosis and medication use was retrieved from those records. The data was analyzed to determine patterns of clinical use of antipsychotic medications. **Results:** Amongs hospitalized psychiatric patients who were being treated with antipsychotic medications in 2005, atypical antipsychotics as monotherapy were the most frequently prescribed (67.6%). Combinations of two or more atypicals were prescribed for 23.1% of patients while 4.4% of patients were on typical antipsychotics and 4.9% was being treated with combination typical-typical antipsychotics. **Conclusion:** The results of this study confirmed the trend of use of atypical and typical antipsychotics.

2. 5th Conference of Asian Association oof School of Pharmacy (AASP), in Bandung, Indonesiaa, 16-9 June 2011

PRO RE NATA PRESCRIBING IN PSYCHIATRIC INPATIENTS

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Background: The use of pro re nata (PRN) medications has been common in psychiatric inpatient care for many years. This practice allows drugs to be administered on patient request or at nurses' discretion for psychiatric symptoms, treatment side effects or physical complaints. **Purposes:** To determine the prevalence of PRN drug prescribing for inpatients at the Adult Psychiatry In-patient Unit, Armadale Kelmscott Memorial Hospital, Western Australia. **Methods:** The medical records of hospitalized psychiatric patients who are treated with antipsychotic medication were reviewed retrospectively. Data relating to medication use was retrieved from those records. The data was analyzed to determine the prevalence of PRN medications. **Results:** In this study, psychotropics were given as PRN drugs were antipsychotic, anxiolytic and hypnotic and anticholinergic medications. Atypical antipsychotic agents most commonly prescribed as PRN use were olanzepine (12 cases) and quetiapine (12 cases). In the typical group, chlorpromazine was the most frequently prescribed drug for PRN use, with it being used for 21 cases. Four patients also were treated with droperidol in PRN use. The numbers of patients receiving anxiolytic and hypnotic drugs as PRN prescription were extremely high. The number of patients getting lorazepam (58 patients) and clonazepam (44 patients) as PRN medications was approximately twice the number cases using these drugs as routine prescriptions (33 and 22 patients, respectively). The number of patients treated regularly with temazepam was similar with those with PRN use (around 40 patients). The use of anticholinergic medication as PRN medication was also high, with 19 patients in this category. Non anti psychotropic drugs that were used as PRN drugs in this study were analgesics, such as paracetamol, panadeine and ibuprofen and salbutamol sulphate inhaler. There were 13 patient treated with paracetamol as needed drug, eight patients with panadeine, one patient with ibuprofen and 10 patients with salbutamol sulphate inhaler. **Conclusion**: The results of this study confirmed the trend of PRN drug prescribing in psychiatric patients. This is a common practice in hospital although this practice contributes to polypharmacy, high doses, side effects and dangerous drug interaction

Keywords: PRN prescribing, psychiatric

Appendix 4 Letter of acceptance for research publication

5th CONFERENCE OF AASP
Asian Association of Schools of Pharmacy
"The Pharmacist as a Key Health Care Player:
The Interplay of Education, Science and Practice"
17-19 June 2011 - Bandung, Indonesia

4 May 2011

Dear Arie Sulistyarini,

We are pleased to inform that your abstract below has been accepted for presentation at 5th AASP Conference

Title: Pro re nata prescribing in psychiatric inpatients

Type of Presentation: POSTER

We will notify you Poster Number and presentation schedule by 6 June 2011.

Please follow the poster specification at 5thAASP conference website.

Thank you and we look forward to welcome you at the 5th AASP Conference.

Best Regards,

Dr. Tutus Gusdinar
Chairman of the 5th AASP Conference
Organizing Committee

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